REGIONAL ILEITIS

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SECOND REVISED EDITION

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Preface to the Second Edition

TWENTY FIVE YEARS have passed since the original paper on Regional Ileitis was read by Crohn Ginzburg and Oppenheimer at the meeting of the American Medical Association at New Orleans in June 1932 Acceptance of the clinical concept throughout the scientific world was prompt and a voluminous literature has since been amassed What was first considered to be probably a rare and unusual disease is now regarded as a malady of wide spread distribution affecting all ages and climes and socio economic strata of the world population What began as a pathologic entity involving only the terminal ileum rapidly evolved to a regional or more diffuse enteritis and was soon expanded to include a generalized ileo jejunitis In more recent years the inclusion of the duodenum and the stomach has been recognized in one published case even the esophagus was cited Combined forms of ileitis and colitis were seen and described as early as 1935 resulting in a confused clinical picture that threatened the concept of ileitis and colitis as being independent and unrelated pathologic and clinical entities

From this small beginning we have witnessed the evolution of a Frankenstein monster that if not threatening to life frequently results in serious illness often prolonged and debilitating Surgery can control this problem fortunately and usually with success

The first edition of this monograph published in 1949 encompassed approximately 300 cases At this writing our experience is based on over 676 cases of diverse types of enteritis with a fairly successful follow up of our personally recorded cases The present study consists of 542 cases of regional or terminal ileitis 70 instances of diffuse ileo jejunitis and 64 examples of so called combined ileo-colitis Thus the writing of the life history of the disease has become a possibility and a proximate evaluation of the medical and surgical treatment which is constantly in a state of flux can at least be essayed as of this date

This new edition is warranted we feel if only for the attempt to bring up to date the follow up of medically treated cases and to ascertain the true figure of recurrences after operation So much has been said of late in the press concerning the effects of treatment (particularly surgical)

in ileitis so many loose statements have been made that a true unprejudiced appraisal is already overdue

The cooperation of my associate Dr Harry Yarnis in collating the clinical data and most important in the follow up of the case has been of invaluable assistance The inclusion of the chapter on Roentgenography by so capable and experienced a radiographer as Dr Richard H Marshak will greatly enhance the value of this book as will the chapter by Dr David A Turner on Intestinal Absorption in Regional Ileitis a subject which truly belongs in the province of the bio chemist

I am much indebted to my confreres at Mount Sinai Hospital for unstinted cooperation and to the medical and surgical profession at large who have made our office a consultative repository of vast amounts of clinical material

June 1957 BURRILL B CROHN M D

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THE TERM REGIONAL ILEITIS was created in 1932 to describe what was considered a new pathologic and clinical entity, a clear cut disease affecting the terminal segment or segments of the small bowel characterized by a subacute or chronic necrotizing and cicatrizing inflammation. While the term regional ileitis is still the most popular denomination of the disease, many other descriptive names have been created by successive authors to cover new and expanding concepts of the anatomic and pathologic aspects of this malady. Terminal ileitis was the first designation because in the original publication the first 14 cases were all restricted anatomically to the terminal 8 to 12 inches of the ileum. Regional ileitis, however, denoted a more widespread distribution. Regional enteritis was suggested by Brown, Bargen and Weber; chronic cicatrizing enteritis by Harris, Bell and Brunn and by Cushway; chronic ulcerative enteritis by Corr and Boeck; segmental enteritis by Lewisohn, to denote both the tendency to scar formation and the more widespread anatomic distribution; while ileocolitis was suggested by Erb and Farmer and again by Colp to indicate the not infrequent involvement of the colon. To this concept was soon added ileojejunitis, the same pathologic process extended to include anatomically all of the jejunum continuously or segmentally. In more recent years the literature has encompassed cases of the same granulomatous process involving the duodenum, the stomach (rarely) and in one case the esophagus. These rare instances are regarded as pathologically identical to that described for the small bowel and require no new terminology. Finally, ileocolitis was created to cover those combined cases where some segments of the large as well as the small bowel are concerned.

As originally described, regional ileitis or enteritis was a nonspecific inflammatory disease, one of the larger group of intestinal granulomata, a process affecting mainly young adults and characterized by an acute, a subacute and a chronic phase of necrotizing, ulcerating and cicatrizing inflammation. The disease is further marked by its tendency to fistula

to the extent of about 18 inches was di tended thickened in the coat externally of a reddish color and internally covered by numerous well defined ulcers varying in size from a diameter of a plit pea to that of a sixpence After a lapse of almost a century the Engli h literature again contained a case report by Moynihan in 1907 entitled The Mimicry of Malignant Disease in the Large Intestine

In the meantime the German literature rapidly began to show an abundance of references to non pecific granulomata of inflammatory nature Braun in 1901 quoted 5 ca es mostly of traumatic or hernial origin and later cited 25 more cases from the current periodical up to 1909 By 1920 Tietze had collated 281 references on this subject including at least 2 cases of typical regional or terminal ileiti (Lowen and also Willman) The literature now increased apace Dalziel con tributed an excellent article and the whole subject crystallized with a paper by Fischer and Lurmann (1933) This paper which included the description of 3 ca es of typical regional or terminal ileiti recognized and granted priority to our original publication le than a year previous in this country [11] The discu ion before the German Congres and there after was amplified by the experience of such noteworthy surgeon as von Haberer Gisbertz Peters Anschutz and Fenster

By 1925 American writers had become cognizant of the subject of nonspecific granulomata of the intestinal tract Coffen in 1925 Horsley (including 2 fine case descriptions of ileitis) and an excellent study by Moschcowitz and Wilen ky (including an admirable photographic repro duction of ileiti) of 4 cases of granulomata of which one was typical of ileitis as we now know it Mock in 1931 summarized the subject of infective granulomata attributing most of these pathologic ma ses to some interference with vascular supply to a given tissue resulting in local necrosis followed by a proliferative reparative tissue reaction He con sidered trauma to be the most common etiological agent His ca es many of them due to penetrating foreign bodies diverticulitis strangulated hernia silk and metallic ligatures involved the sigmoid stomach omen tum splenic flexure and in one case participation of the terminal ileum Golob added one case and Erdmann and Burt 5 more 2 of which had typical involvement of the terminal ileum with intestinal obstruction and internal fi tulas from ileum to cecum Finally in 1933 Ginzburg and Oppenheimer reported a group of 52 instances of nonspecific granulomata of the inte tinal tract these cases were the result of vascular di turb

formation within adjoining loops of the small and large bowel by external fistulas to the abdominal wall and by frequent rectal suppurative complications A disproportionate increase of connective tissue may and frequently does lead to intestinal stenosis and obstruction Clinically the disease is featured by fever diarrhea loss of weight a secondary anemia and the formation of an intra abdominal mass constituted by approximated loops of inflamed intestine frequently joined together by internal fistulas The process regularly begins or stops at the ileo cecal valve the exceptions to this localization being few in number The disease may extend upward by skip lesions separated by healthy skipped areas It is rarely a progressive lesion it may remain for twenty or more years strictly localized in the terminal ileum Progression of the disease and involvement of nearer or higher areas frequently result after attempts at surgical cure the original focus of disease if not molested may increase in intensity and severity but will not extend in an anatomic progression Recurrences of the inflammatory process after palliative or radical surgical procedures further characterizes the process as an active persistent and recurrent disease

Historical Background

Nonspecific granulomata of the alimentary tract involving mainly the large bowel have been recognized for many years The great pathologist Morgagni (1682 1771) in his De Sedibus et Causis Morborum reported cases of enteritis with particular involvement of the ileum as pointed out by Hymen I Goldstein The European medical literature has been replete with innumerable examples of such inflammatory masses located in large and small intestine some even in the stomach included in these descriptions undoubtedly are many instances of what we recognize now as typical ileitis or enteritis In 1813 Combe and Saunders reported before the Royal College of Physicians of London A Singular Case of Stricture and Thickening of the Ileum To quote in part The lower part of the ileum as far as the colon was contracted for the space of three feet to the size of a turkey quill John Abercrombie discussed pathologic states of the ileum and reported cases very similar to regional ileitis His description published in 1828 is instructive A girl aged 13 about a year before her death (1814) began to be afflicted with pain of the abdomen and frequent vomiting The caput coli 3 inches along the ascending colon and the lower end of the ileum

Three years after the first designation of regional enteritis as an entity Binney was able to collect 267 cases from the literature in 1939 Ravdin and Johnston catalogued 393 cases from current periodicals Confirmatory reports from the English literature were not long in making their appearance (Jackman Hadfield Barbour and Stokes Molesworth Hurst and his co authors) as likewise from the Dutch literature (Groen and Pompen Snapper Pompen and Groen)

A dissident viewpoint was advanced by several writers who considered regional ileitis a clinical but not a pathologic entity because of the occurrence of the disease at various other areas of the intestines Characteristic lesions involving the jejunum were shown in 2 cases (Harris Bell and Brunn) of 18 cases reported from the Mayo Clinic in 1934 (Brown Bargen and Weber) the ileum was involved in 9 the jejunum in 3 the terminal ileum and parts of the colon in 6 instances Homans and Hass while recognizing typical terminal ileitis questioned the localization of the process and felt that the jejunum was more often involved than was then recognized They thought that the appendix was possibly an important etiologic factor they further remarked for the first time that the disease might have a predilection for Hebrews (Mixter) a theory that has since been disproved Meyer and Rosi emphasized the involvement of the mesentery particularly in fistula formation Erb and Farmer emphasized the acute phase in children as it simulated appendicitis Reichert and Mathes made the first suggestion regarding etiology namely experimental lymphoedema by blocking lymphatics Goldfarb and later Kantor gave the first veritable description of the roentgen appearance of the disease in the terminal ileum as the string sign

Actually considerable knowledge has been added to the original concept of terminal or regional ileitis in the last twenty five years The anatomic and pathologic states have been extended to include the upper reaches of the ileum and all of the jejunum even duodenum and stomach opportunity has been afforded for studying the life history of the disease its progression and extensions Acute ileitis if such a concept exists has been analyzed and its subsequent course has been traced Above all prognosis has been learned and finally medical and surgical approaches to therapy have been tried some discarded newer method apprehended The whole problem of recurrences with their increasing frequency and severity has had to be acknowledged and a rational method of recognition and treatment of these recurrences has been attempted

ances herniation and sealed-off intestinal perforations and included several examples of the entity which had already been isolated and termed regional ileitis

This large group of nonspecific inflammatory granulomata involved any or all parts of the alimentary tract and omentum They formed masses often obstructive in nature that usually simulated in their clinical course the picture of a new growth They were characterized by a piling up of granulation tissue with various stages of ulceration necrosis and fibroblastic proliferative secondary reactions The histologic process consisted of round cell infiltration fibroblasts connective tissue stroma and new blood vessel formation with the occasional occurrence of giant cells of unusual magnitude (Moschcowitz and Wilensky) Etiologic agents apart from trauma and foreign bodies were not recognized tuberculosis syphilis and actinomycosis were excluded by definition

Regional Ileitis [4]

From this large and general group of nonspecific granulomata of the intestinal tract a subspecies termed regional ileitis was isolated a distinction which was possible because this group was characterized by a consistent anatomic distribution a characteristic clinical course a progressive life history and typical complications of fistula formation and obstruction Also this group was further amenable to successful surgical interference It is interesting to note historically the amplification of the original concept of terminal ileitis The first report covered 14 cases of a typically characteristic disease involving only the terminal segment or segments of the ileum Acute cases were included among those running the more easily recognized chronic inflammatory course Shortly there after (1933) the involvement in some cases of the upper reaches of the ileum and all or part of the jejunum as noted by Harris Bell and Brunn led to the identification of ileo jejunitis either as an extension or a continuation of terminal ileiti or as a ubgroup per se in which the involvement of the terminal egments of the mall intestine was sub ordinated to the proce s higher up The participation of the colon segmentally either by contiguity from the terminal ileum or by scattered areas of coincidental disease wa fir t noted by Colp (1934) and sub sequently by Crohn and Rosenak (1936) and led to the creation of still another subgroup ileo colitis (Crohn and Berg) denoting a most confused and complicated pattern of involvement of ileum and varying segments of the large bowel

becau e of their own identifying characteri tics though some confusion will arise when attempts are made to separate true primary acute ileitis from acute exacerbations of chronic recurrent ileitis In fact some doubt has been rai ed as to whether such a syndrome as acute ileitis does actually exi t or rather that such acute manifestations really repre ent sudden exacerbation of a smoldering chronic pathologic state

The group of ileo jejunitis and duodenitis has been considered separately becau e the involvement of the whole or of mo t of the small bowel introduces new elements of clinical significance and misses many of the di tingui hing characteristics of the terminal form Its life history is different its therapeutic approach is entirely singular its differential diagnosis and progno is call for a more novel viewpoint The fourth category of combined ileitis and coliti is so confusing with so many cross elements and complications and is so difficult a problem in therapy particularly with regard to succes ful surgical treatment that it requires its own generic consideration

The truly encyclopedic review and experience at the Mayo Clinic published in 1954 by Von Patten et al encompassing an extensive group of 600 cases, represents a massive addition to our present knowledge of the disease particularly valuable is the superb follow up of their cases over many years which is incomparably complete

Scope of the Present Study

This study is an analysis of instances of segmental enteritis which have been under our own personal office and hospital care during all or part of the last twenty five years These cases are all private patients who have been observed carefully treated and subjected to continuous analysis including follow up during this period Some were included in the original group that constituted the first 14 cases published in 1932 as terminal ileitis The remainder have been registered during all of the succeeding years the last addition to the list having terminated approximately six months ago (January 1957) to allow for some albeit inadequate follow up Ward cases in hospitals are not included those that are listed were accepted only becau e they olicited treatment and were registered as personal patients even though the previous surgical or medical treatment had been administered elsewhere For purposes of analysis and study this larger group may be subdivided into four essential categories (1) Regional Ileitis—the acute and chronic forms 542 cases (2) Ileo jejunitis 64 cases (3) Involvement of duodenum and stomach 6 cases (4) Combined ca es—ileitis with involvement of some of the large bowel 64 cases (To al 676 case)

All four categories represent types of regional or cicatrizing enter itis They are not di tinct entitie in fi t mixed forms are not unusual The identical pathogenesis and pathologic hi tology is common to them all But they differ sufficiently clinically and anatomically to merit con sideration as separate group each group has identifying characteristics its own life hi tory and progno is as well as its individual approach to therapy

The large t group of case of ileiti comprises the bulk of the study and provides the greatest number of the cla sic variety of the di ease in which the ileum particularly the terminal egments of small bowel i involved The disea e being one of low grade pathogenicity and chron icity requires that this group be identified as chronic regional ileitis In contradistinction the acute case have been separately con idered

and chickens and proved negative in 5 of the original cases Subsequently whenever a suspicion of tuberculo is has ari en the mo t careful pro cedures have been followed to eliminate the Koch factor as an etiologic agency When tubercle bacilli have been demonstrated in cut sections or when guinea pig inoculations have been positive the case has been considered as intestinal tuberculo is simulating ileitis Frazer and Haggar reported a case of regional ileitis resected in which the mesenteric lymph nodes showed old caseating tuberculosis the specimen of ileitis itself was free of any evident inva ion by the tuberculous proce s and was nonspecific granulomatous in nature by hi tologic study A total of 762 cultures and 131 inoculated animal including guinea pigs rabbits cats chicken and rats with material from lesions of 43 patients failed to give positive results for mycobacterium tuberculosi (Van Patter)

Syphili and actinomycosis two specific infections that may involve the intestine have been excluded as an etiologic agency becau e of the fact that serologically syphilis and histologically actinomycosi are easily differentiated and excepted

Specific Agencies

Many authors have found various b cteria in cultures of tissues or in peritoneal exudates and have implied that these bacteria were the etiologic agents of the di ease This occurred many times in the earlier publications after the disease was first described recent literature has made no such claims and no such confutations Frb and Farmer in one case found in stained sections of the involved gut gram negative bacilli apparently of the B coli group By culture they obtained a similar organ ism from the ileal mucosa mesenteric lymph glands liver and bile In their comment on the finding Ravdin and Johnston point out that these tissue cultures were taken eight hours after death and that no specific agglutinations against the patient s blood had been es ayed Ro s has found similar bacteria in one case an anaerobic streptococcus from the peritoneal fluid from the mesenteric lymph nodes and from the deep surface of the intestinal ulcerations Peters found the usual enterococcus of intestinal type in the cultures of superficial tissue but no bacteria in the sections of deeper ti ue Jackman in 2 cases of acute *ileitis was no* able to demonstrate bacteria in the deeper layers of the resected specimens Others have found gram positive cocci in the submucosa (Konjetzny) enterococci in stool cultures (Fischer and Lurmann) aerobacteria aero

Chapter 2 Regional Ileitis Etiology (542 cases)

REGIONAL ILEITIS is a non specific chronic recurrent granulomatous *disease, affecting mainly young adults and characterized by a necrotizing ulcerating inflammatory process one in which cicatrizing elements in* the long enduring cases is an important feature The terminal ileum is *apparently the parent seat and origin of the pathologic process though the whole ileum may be involved Typically the process rests at the* ileo cecal valve transcending that barrier only exceptionally Clinically *the disease is marked by a low grade fever abdominal pain most frequently by mild diarrhea and by progressive loss of weight and a secon*dary anemia The occurrence of an intra abdominal mass is frequently *noted The most striking clinical feature is the formation of fistulas of ileal origin these fistulas leading from ileum to the abdominal wall* or from ileum to other loops of bowel or other hollow viscera Rectal complications of a suppurative nature constitute a striking manifestation of the disease *The pathologic process is an enduring one lasting over* the course of many years Eventually intestinal obstruction and hemor*rhage may intervene open perforation of the small bowel is extremely* rare *Spontaneous cures are minimal but may often occur* surgical intervention is still *the therapeutic method of choice*

ETIOLOGY

The true causation of ileitis remains unknown despite diligent efforts to ascertain a bacterial or specific agency as the factor in its initiation It was of first importance to exclude tuberculosis as the specific *infecting* agency Much confusion in the past has evolved from the inclusion of cases of *non specific ileitis* within the category of hyper*trophic ileocecal tuberculosis All resected specimens of ileitis* have been conscientiously subjected to careful histologic study careful *staining* methods for the recognition of the Koch bacillus in cut sections to cultures and animal *inoculation*

Material from the bowel *wall of the ileum* and from mesenteric nodes *in the early resected cases were inoculated into guinea pigs* rabbits

Protozoa

The entamoeba hi tolytica was implicated by Corr and Boeck on the ba is of one case finding However the typical pathologic lesion of amebiasi were absent from other segment of the large bowel as is characteri tic of amoebic infestation No other authors in the literature have made similar claims In other in tances Trichocephalu dispar Oxyuris vermiculari Giardia lamblia and other para ites have been found in the stool examinations but never sufficiently consistently as to imply that their presence was the cause of ileitis

Foreign bodies which play so large a role in granulomata of the intestinal tract such as fish bones metal ligatures food residues pits and fragment of bone are ab ent from cases of true regional ileitis or jejunitis Large giant cells are regularly found in histologic sections of ileiti these giant cell are not tuberculous or syphilitic in origin They are best explained on the basi of foreign body inclu ion but the ex traneou substances that give rise to such giant-cells are not gross or material in substance They are probably in some in tan e due to (a) lycopodium spore from dustings of surgical gloves or a previous surgical intervention or to (b) minute fragments of food detritus collected and secondarily caught in the ulcerated pockets of the mucosa

Bacillary Dysentery

Felsen claimed a common source of origin for a large percentage of the cases of di tal ileiti chronic ulcerative coliti and nonspecific granulomata This concomitant agent was in hi belief the Shigella dysenteriae In a follow up of 400 cases of acute bacillary dysentery he found 29 cases of acute distal ileitis 22 cases of chronic di tal ileitis 18 cases of combined chronic ileo-coliti and 84 cases of chronic ulcer ative colitis His study included a survey of the late end results of the epidemic of bacillary dysentery which occurred at Jersey City in Septem ber 1933 He gave 84 cases with high serum agglutination against Shigella dysenteriae and 8 with positive stool culture He describes particularly an acute dysenteric appendicular form with involvement of the small bowel and various types of mixed forms involving terminal ileum and colon Hi clas ification and acceptance of dy entery i based upon agglutination titers of 1 100 and over except for the Sonne Duval type in which he accepts 1 50 as significant Po itive stool cultures were obtained in 10 of 70 cases examined

genes (Halligan and Halligan) Mailer found streptococcus viridans in 2 of his cases

These various observations are of interest but fail to give consistent findings which would regularly implicate a single causative bacterial agency Numerous attempts by staining by aerobic and anaerobic cultural methods and by animal inoculations have similarly failed to uncover a singular offending agency

A most serious attempt to investigate the bacterial etiology of the disease was made by Pumphrey at the Mayo Clinic Thirteen cases of granuloma of the bowel were studied 10 of which were typical regional ileitis Cultures were taken by sterile technic in the operating room from resected specimens and regional nodes The specimens were macerated and planted in media such as blood agar eosin methylene blue plates dextrose brain broth chick mash overlayed with paraffin and agar slants Many organisms gram positive and gram negative were recovered none of which could be said to be predominant throughout the series In no instance was he able to isolate an organism of the dysentery group None of these bacterial cultures were consistently agglutinated by the serum of the patient from whom the culture had been obtained nor by the serum of other patients suffering from the same disease Cultures from the throats of 2 patients with the disease yielded streptococcus viridans the injection of these cultures into rabbits failed to reproduce the disease Exhaustive studies for tubercle bacilli and for spirochetes were similarly negative

Johne s disease in cattle has many resemblances to human ileitis in its anatomic configuration except that the former is regularly demonstrated to be associated with a specific microorganism the Mycobacterium johnei Williams injected johnei subcutaneously into patients with regional ileitis and also into normal controls without establishing any casual relationship between ileitis and Johne s disease Emsbo in Denmark described porcine ileitis occurring in swine frequently in more than one of the numerous litter This disease which occurs spontaneously in Denmark has many striking anatomic and histologic characteristics very similar if not identical with human ileitis Tuberculosis was absent The multiple litter incidence and intestinal fistula formation are common with ileitis as we know it in human clinical material

A thorough search by veterinary pathologists of the Canadian Government has failed to elicit any trace of a similar porcine disease in Canadian swine (Turner)

small intestine lower and mid ileum by a granulomatous infiltration having all the histologic characteristics of ileitis or of nonspecific granuloma in a Negress bearing the obvious perineal and vulval lesions of lymphogranuloma Five lesion were found in the upper and more proximal part of the ileum the lowermost being 6 inches from the ileo-cecal valve The wall of the bowel was thickened the lumen dilated and the mucosal surface was granular and showed numerous shallow ulcers

However from thi exceptional case of lymphopathia venereum with involvement of the ileum no conclu ion can be drawn regarding ileitis as a viru di ease at lea t not a the identical virus of the Nicholas Favre disease My own attempts to obtain a positive Frei test in ileiti have been unsuccessful The frequency of recurrences in ileitis even after exten ive resections and the inability to demon trate a specific bacterial agency allow one to maintain an open mind on the possibility of a virus with a predilection for the ileal mucosa The fact that the two observers did find involvement of the ileum in lymphopathia venereum suggests that a similar though not identical virus may be considered as a pos ible true etiologic agency in ileiti More and more as time passes and no po itive etiologic agent can be identified the possibility or the probability of a viru agency becomes the more plau ible

Allergy has been suggested by Tallroth as the etiologic agent he described 2 case historie of ileiti allergica The finding of many eo inophil in the hi tologic sections wa repeatedly stressed and obviou ly constitutes the basi for hi suggestion The vascular injury was also typical of an allergic granulomatous proce s He regard the pathologic proce s in ileiti as a local anaphylactic reaction in the nature of an Arthus phenomenon

Sarcoidosis

The histologic pathology of Boeck s sarcoid and of ileiti i almost identical Homans and Ha stres ed the similarity in lymph gland pathology in the two di eases Longcope and Pierson in their review of sarcoidosi make no reference to intestinal le ions Williams and Nickerson review 4 cases of sarcoidosis but without any ileal intestinal or colonic involvement Snapper reviewing the pathology clinical incidence and histology of the two diseases terms them pseudo-tuberculosis in nature In their respective clinical manifestations however he differentiates sharply between them considering them unrelated in all aspects

The findings and implications of Felsen so often quoted in the literature may be variously criticized The agglutination in the serum of patients against recovered organisms and against type laboratory cultures are today open to the criticism of nonspecificity The small number of positive stool cultures (10) recovered after an epidemic of acute dysentery is not significant for ileitis

In our own series of almost 700 cases and in the experience with the additional ward cases at the Mount Sinai Hospital over a period of over 25 years I can recall only 2 cases with a transient positive culture for the Flexner type of dysentery and only an exceptional case with high agglutinations against similar bacteria In only one instance an agglutination of 1 320 against Hiss was reached

The imputation that regional ileitis or ileo jejunitis is regularly caused by the Shigella dysenteriae has not been substantiated and is not acceptable to most authors

Viruses

The virus of lymphopathia venereum has been suggested as the cause of ileitis Stafford in 10 cases of lymphopathia venereum found 3 patients suffering from a form of segmental colitis in no case was the small bowel involved Because of the cicatrizing tendencies and the possible similarity to cicatrization found in the rectum in lymphopathia venereum Koster and his associates carried out the Frei test in 4 cases of resected ileitis and in 2 others of ileitis not resected with negative results Rodaniche Kirsner and Palmer considered that the two diseases resembled each other in the primary lymphatic involvement and later development of severe stenosing lesions However in 4 cases of ileitis the Frei test was negative with mouse and human antigens The serum was also found negative for neutralizing antibodies against the virus Similar negative results were found by Friedl Meyer However Llombart and Mayern described a case of lymphopathia venereum with multiple stricture of the ileum as well as a rectal stricture Ocular manifestations were also present confirmatory of the virus type of infection Coutts and Opazo in a study of several cases of lymphopathia venereum were able to demonstrate only one instance with ileal involvement In this person there was an extensive proctitis and an ileitis involving a large part of the terminal ileum

Likely and Lisa give a detailed report of an involvement of the

case of granuloma the direct result of an accident such as from an automobile or a fall was ever reported He makes an exception of course for granulomata resulting from tears of the mesentery from direct violence to the abdomen foreign bodies splinters of wood strangulated hernias and residual suture material However as early as 1936 Reichert and Mathe cite the case of a man who suffered a stunning blow to the abdomen from the steering wheel of his automobile Two weeks later he developed severe abdominal pain with vomiting and diarrhea Later resection of the ileum revealed a granulomatous lesion twelve inches in length which was proximal to and not occupying the usual site for regional or terminal ileitis

Two cases of regional enteritis following external trauma have been reported from the Mayo Clinic In one case three months prior the patient had had an accident while horseback riding in which his mount had fallen on him delivering a severe crushing blow to the abdomen On exploratory operation some weeks later an obstructing lesion was found about 7 feet from the ileo cecal valve relief followed a short circuiting procedure Later the lesion was resected

The second case involved a farmer who four months previously had been caught between two heavy farm implements sustaining a pulverizing injury to the abdomen At operation several loops of ileum were bound together by inflammatory adhesions and were fixed to one loop of lower jejunum which was definitely obstructed The usual edema of the mesentery and enlarged lymph nodes and fistulous tracts so characteristic of ileitis were absent These cases do not resemble ileitis in anatomic distribution or in symptomatology They represent true direct trauma to the small intestine with resultant granulomata and obstruction Nominally they are instances of ileitis of traumatic origin

Ten Kate in 1936 reported 2 cases of regional enteritis following severe trauma In one a rupture of the ileum was found at operation though nothing that resembled clinical ileitis the other a characteristic lesion with a fistula from the ileum to the bladder was observed at operation

Spellberg and Gray cited the case history of a soldier motorcyclist who ran into the end of a stalled truck Abdominal pain and vomiting supervened within thirty days X ray revealed a typical jejunitis beginning just below the fossa of Treitz At operation the jejunum resembled a garden hose being indurated and edematous with accompanying enlarged lymph nodes Resection of the lesion was eventually required

More recently isolated sarcoidosis of the small intestine simulating nonspecific ileo jejunitis has been described This is the first instance in which the real differential diagnosis of ileitis from sarcoidosis involving the small bowel has been verifiably noted though in the literature small intestine involvement has been occasionally suspected In this paper by Watson and associates 2 case histories are detailed which require analysis The radiographic picture resembled ileitis or ileo jejunitis Resected specimens had many of the characteristics similar to those of ileitis except for polyposis the histologic picture was almost identical Hadfield in studying 20 cases of ileiti had found 13 in which epitheloid cell tubercles were present and cautiously suggested the identity of ileitis and sarcoidosis

Moreland has published an article entitled A case of sarcoido is of the lung with regional ileitis A filling defect of the cecum was observed radiographically At operation resection of the terminal ileum was performed Typical changes of a sarcoid nature were histologically observed in the removed mesenteric lymph nodes This case is not convincing as one of ileitis It could very well however be a good example of involvement of the ileum and colon in sarcoidosi

The generalized picture of sarcoido is in all its clinical manifestations including skin and pulmonary le ions and the ab ence of fistulas string sign and rectal complication have convinced most authors that the two diseases bear little relationship The most that can be aid is that sarcoido is may occa ionally show involvement of the small bowel Bernstein Konzelman and Sidlick report a case of Boeck s arcoid with true involvement of mucosa of the ileum marked by thickening of the wall with ulcerations measuring 2 x 4 cm In the ca e of Lenartovicz and Rothfeld the ga trointe tinal tract was diffu ely involved Homan and Has stated that ome ob erver have called ileitis sarcoid of the small intestine Warren and Sommers collected the reports of 50 cases of arcoido is with complete autop y studie in 7 of the e ca es intestinal lesions were de cribed Three of the e howed generalized involvement throughout the stomach and bowel an i olated lesion in the ileum was not de cribed Twenty one ca e of proven sarcoidosis were studied by radiography in *no* in tance wa an abnormality encountered suggestive of gastrointestinal involvement (al o Lorber Shay and Wolo hin)

Trauma

Mock (1931) in discu ing infective granulomata states that no

fistulous tract to the cecum and adjoining loops of the small bowel. The patient was observed for two years during which time successive x-ray showed complete and spontaneous resolution. The mass in the deep abdomen disappeared under observation.

The lifting of the weight, while not the cause of the ileitis, was most probably a factor in bringing to light a latent and asymptomatic regional ileitis.

Case [illegible] M.J. A man [illegible]5 years of age, while in the armed services, was severely stunned by the explosion of a bomb on board a U.S. destroyer. Upon recovery he began to complain of abdominal pain and diarrhea. The radiographic picture upon his discharge was typical of ileitis. Nevertheless he was able to continue in the armed services and obtained an honorable discharge. Under observation, the symptoms and radiographic evidence of ileitis have subsided and his case is considered one of spontaneous cure.

Case 6. C.G. A man in an auto accident was thrown violently against the steering wheel of his car with severe bruises to his abdominal wall. Two months after the injury he developed diarrhea and abdominal pain and lost 30 pounds in one year. A resection of the terminal ileum revealed a typical regional ileitis. He was well after the operation for 3 years when he again suffered an accident, this time being hit by a streetcar and thrown violently backward. Immediately the diarrhea recurred. A recurrence of the ileitis in the loop of ileum proximal to the previous anastomosis was suspected though not proven.

In the last ten years we have added 6 more cases wherein trauma seems to have been either an initial factor in the causation of the ileitis or in the aggravation of a possibly pre-existent disease. In one case a violent fall upon the abdomen immediately preceded the onset of symptoms. In 4 other cases an automobile collision, usually of the head-on type, immediately preceded the initiation of symptoms and seemed scientifically and logically to be responsible for the causation or aggravation of the intestinal disease. In another case of quiescent ileitis the fracture of a finger was immediately followed by a recrudescence of all intestinal symptoms. With the increasing number of automobile collisions, particularly of the head-on variety, the question of the relationship of trauma to intestinal diseases comes more and more to the foreground. In a head-on accident the body of the driver is violently catapulted forward, the lower thorax and the abdomen striking the steering wheel. The subsequent development of abdominal symptoms raises both the point of the origination of a visceral disease and of the aggravation of

In my own experience in spite of initial skepticism there seems to be sufficient basis for associating trauma and ileitis in the relationship of cause and effect (Crohn) This conclusion is based upon experience with the following six cases briefly abstracted

Case 1 S 4 A man 39 years of age in an automobile accident was violently thrown forward against the steering wheel of his car sustaining severe abdominal trauma Abdominal cramps and diarrhea supervened almo t immediately though the man had previously always been well Operation performed less than two weeks later because of the severity of the complaint revealed a typical terminal ileitis cured by resection The patient received a large award from the courts This was my first experience of that type as an expert I testified against the likelihood of trauma creating such a lesion as ileitis though I was unable to deny the p obable aggravation of a pre existent latent lesion My viewpoint was changed by the ucceeding experiences

Case 2 J 4 A boy 17 years of age always previously well was thrown violently across the aisle of a bus as it was involved in a collision striking his abdomen on the forward seat He immediately developed hemateme is and symptom of a traumatic duodenal ulcer A gastro entero tomy was performed a few weeks later the stoma functioned badly At re operation a typical regional ile tis was noted and resected It seems reasonable to deduce that both the duodenal ulcer and the ileitis which involved the terminal loops of the small bowel were traumatic in o igin

Case 3 M M A 26 year old man suffered at 3 years of age a profound trauma when struck by a moving truck The child immediately developed an ab ces in the right lower quadrant of the abdomen requiring seve al operations and characterized by an obstinate fecal fi tula to the abdominal wall When he wa 8 year of age the previously closed fi tula reopened pontan ously and remained open for several months Four year late the fi tula again reopened but closed without surgical intervention The ame equen e of e ent to k place four years ago For the la t ten month the patient ha pre ented the typical symptom of regional ent riti w th dia h a fe er and abd minal pain Two fecal fistulas are pre ent on th nt r abdominal wall

Case 4 H 1 A woman 50 yea af ag lifted a h avy object and immediately felt a pa n in the r ght lowe quadrant of the abdomen She suffered no diarrh a or fev S ven weeks late on phy ical examina tion a tender sau ag haped ma wa noted in the right lower quadrant of the abd men Rad ographi ally a lear c t p cture of ileitis wa seen involving 1 to 18 nche of th t rminal l um w th seve al sho t

several such striking examples are of such interest as to merit closer analysi

In 1934 the first in tance of ileiti occurring in sibling was pub li hed A boy of 14 who represented historically a very early clinical history of ileitis was resected and the diagno is firmly established Two years later his 32 year old sister complained of abdominal pain and vomiting and developed signs of intestinal ob truction At operation a typical ileitis involving the terminal 8 inches of small intestine was resected The anatomic situation and pathologic attributes of the lesion were identical in both siblings

In this present study we have encountered 12 instance of familial involvement

REGIONAL ILEITIS

Rel tionship	*No of Cas s*
Brothe and brother	2
Brother and i te	3
M the and s	2
M the nd daughter	4
First c u n	1

In two other brothers one had ileitis resected the second was a case of typical ulcerative colitis Mother and daughters constitute a different group which was seen four time all the cases being confirmed In another instance the mother had ileiti the daughter ulcerative colitis In a fourth instance the child had ileitis and the mother and two maternal aunts of the child had ulcerative colitis We have again noted an uncle suffering with ileiti his niece with segmental or right sided colitis

Three family groups further afford a striking picture In the first a young woman her brother and her half brother all have ileitis the father is sufferin from ulcerative colitis In the second family group we note ileiti segmental colitis and ulcerative coliti in 3 adult siblings (fig 1) In the third family group a child and her two aunts by con anguinity have all had ileitis confirmed by operation Bockus refers to two cou ins suffering with regional ileitis with extension into the colon ileocolitis both resected and well they had previously lived together in the same hou e Brown and Schiefly have reported regional enteriti affecting 3 siblings 2 sisters and one brother In 2 of the siblings the colon wa involved as well as the terminal ileum A case of regional

a pre existing disea e This type of accident applies with some reason in instances of low grade ileitis and such cases are becoming increasingly common in the courts

Ileitis i a di ease of great chronicity often latent for years In the analysis of case histories in general it is not unusual to read of mild almost negligible occasional complaints for 5 10 or 20 years before the eventual diagnosis is established Nor is diarrhea a constant clinical symptom in ileitis or enteritis The thought seems therefore justifiable that in these instances where trauma has been related to ileitis actually one is dealing with an aggravation of a pre existent latent ileitis However the cases from the Mayo Clinic and the first 3 cases in my personal experience seemed sufficiently well checked and proven to allow the inference that the trauma preceded and cau ed the intestinal lesion In the other cases the aggravation of i le ion by the trauma eems justifiable

Traumatic enteritis in its clinical course i identical with ileitis as we know it in its well recognized forms Abdominal mass fi tula formation diarrhea and fever are all present Segment other than tho e of the terminal ileum are more likely to be affected by the indiscriminate application of the trauma

Spontaneous resolution was twice observed an incidence that would seem higher than in the control nontraumatic cases

In discu sing the relation hip of trauma to internal di eases Loniger and Molineus have laid down the following four dicta

1 It mu t be shown that no prior disease had existed
2 The trauma must be sufficient to act as a po sible cau ative factor
3 The active symptoms must follow directly upon the trauma
4 The clinical symptom must be identical with that of the disease (Brahdy and Kahn)

In most of the quoted case of trauma followed by ymptoms of ileitis the e four dicta have been truly fulfilled

Familial Incidence of Ileitis as a Possible Etiologic Factor

Ulcerative colitis non pecific a i ter di ea e rarely occurs in more than one member of a family My own experience and medical literature in general bear out that fact On the other hand regional ileiti or enteriti occurs in multiple instance in intimately blood related members of a family sufficiently often to warrant attention becau e herein may lie a clue if not to etiology at least to familial pre di po ition My note on

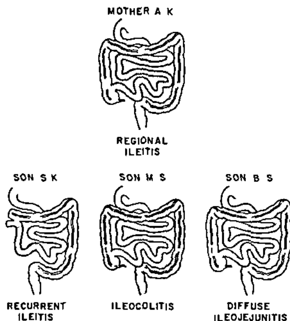


FIG 2 Familial incidence in one family

of ulcerative colitis one could understand contact infection such as occurs in epidemics of bacillary dysentery or in amoebiasis by finger transmis ion or by insects particularly flies Or one could conceive of a common vector Since such a specific etiologic agent is not known it seems more logical to fall back upon at least a familial predisposition to the unrecognized infective agency such as factor predisposing to ileitis to ulcerative colitis or to both diseases The mixed cases of ileo-colitis seen in this series again only draw attention to the common liability of small and large intestine to the offending agency or agencies

Theories Regarding the Pathologic Mechanism in the Creation of Ileitis

Most of the hypothetic considerations regarding the actual location of the lesion and the po sible direct physical factors in initiating the granuloma have centered about the terminal ileum and ileo cecal valve *This view point ignores the fact* that the lesion may occur at any level of the small intestine and also that recurrences of ileitis occur far from

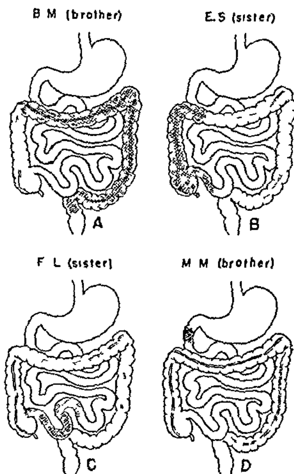


FIG 1 Familial nciden e n f ur blings
A *Ulcerative Col tis* B *Segmental Col ti (ight sided)* C *Regional Ileit s* D *Duodenal Ulcer*

ileitis in a father and on hi also been de cribed Heard and John cite a more recent case of chronic ileiti in a mother confirmed by exploratory operation Two years later her child 7 / year of age was operated on for an acute ileitis

The significance of the e finding remains conjectural they are too interesting however to be di mi ed without con ideration If a proven bacterial or viral agency could be incriminated as the cau e of ileitis or

compromised by undergoing rotation Bell however in experimental studies could not reproduce granulomata by interference with the blood supply

The Theory of Lymphatic Block

Of much greater interest is the question of the relationship of the mesenteric lymph glands and the lymphatics of the intestinal wall to granulomatous ileitis The constant finding of enlarged lymph nodes in the mesentery of the affected loops of intestine while easily explained on the basis of secondary infection has caused some writers to advance the hypothesis that the primary lesion may be resident in the lymphatic tissues the organic changes in the wall of the gut being secondary thereto Holman in discussing a paper by Bell in 1934 asks whether the lymphatic hyperplasia is an expression of a chronic infection originally in the bowel or possibly the primary lesion with subsequent fibrosis and secondary constriction of the intestinal canal Two years later Reichert and Mathes published a paper on Experimental lymphedema of the intestinal tract and its relation to regional cicatrizing enteritis The dominant features of the intestinal lesion in ileitis resembled a low grade infection with a concomitant chronic lymphatic obstruction and edema They observed the pathologic resemblance to elephantiasis as seen in the extremities of the body In animal experiments sclerosing substances were injected with a fine needle into the mesentric lymphatics and serosal lymphatics of the wall of the intestine

The material used for sclerosing purposes included crystalline silica mesh bismuth oxychloride indelible lead or sodium morrhuate In some animals a 24 hour broth culture of B coli was given intravenously one to three hours before the lymphatic injection those bacterial injections occasionally being repeated at intervals subsequent to the acute experiment When the animal was killed the treated segment of bowel felt thickened some of the mesentery lymphatics were dilated some sclerosed free peritoneal fluid was not present The thickened bowel wall showed inflammation and thickening of the serosa edema of the circular and longitudinal muscle fibers the submucosa was swollen and infiltrated with leukocytes the mucosa swollen but not ulcerated Chronic pathologic changes persisted without subsidence for months after even a single sclerosing injection The changes were seen in all specimens (12) examined but were most marked in those experiments in which bacterial suspensions were intravenously injected coincidentally

the original site of inflammation and from the valve of Bauhin Naturally the first suspicion was directed at the appendix as a causative factor Many writers have suggested that a fibrinoplastic process beginning in the appendix extended to the ileum thus constituting terminal ileitis (Lowen) Fischer made the same claim but this time through the mediation of the mesenteric lymph nodes Ravdin and Rhoads again pointed out the similar pathologic changes in fibroplastic appendicitis and the chronic stage of regional ileitis Homans and Hass and Erb and Farmer suggested primary appendiceal disease as an etiologic factor

In refutation of this idea it should be noted that the appendix had previously been removed in over 25 per cent of cases of ileitis The life course of the disease is in no way altered or stayed The resected appendix apart from showing slight chronic changes of the usual type seen in adult life is free of typical granulomatous changes such as characterize *granulomata and ileitis In this series we encountered only six* instances of grangrenous appendicitis either during the active phases of the disease or subsequent to short circuiting procedures Nor is there reason to expect the appendix to be involved in ileitis since the appendix originates from the base of the cecum beyond the ileo-cecal valve and is separated anatomically from the ileum by the ileo cecal valve which is such an efficient barrier in preventing the spread of the ileitis to the cecum Nor does acute appendicitis occur more frequently in the combined cases with cecal involvement Histologically the appendix in the resected specimens of combined ileo colitis does not participate in the peculiar and characteristic granulomatous inflammation

Vascular Changes

The analogy of ileitis with intestinal granulomata might well suggest that the similar pathologic picture in both diseases results from an identical impairment of the blood supply Those authors who have written on the subject of granulomata of the intestinal tract have emphasized volvulus intussusception strangulated hernia and traumatic rents as direct causative agents leading to granulomatous mass formation Ginzburg and Oppenheimer [8] particularly stress the reduced vascularization that results in mucosal necrosis ulceration and secondary hyperplastic granulomatous change Barbour and Stokes mentioned the possibility of a chronic recurrent intussusception Bockus and Lee discussed the peculiar blood supply of the terminal ileum and its mesentery suggesting that the terminal branch of the ileo-colic artery might be

The possible relationship of acute mesenteric lymphadenitis to acute and chronic regional enteritis presents an interesting thought Jackson suggested the kinship of the two diseases However in 15 cases he found only a mild hyperemia of the terminal 3 to 4 inches of the terminal ileum he has no record of any case of ileiti originating in or from mesenteric lymphadeniti Rockey roted thickening of the ileum in children with acute mesenteric lymphadeniti in 4 cases All were valid case of acute ileitis with marked lymphadenopathy and this in September 1932 before the first publication on ileiti

On the other hand Eliason and Johnson state that they know of no case of acute ileiti originating in acute mesenteric lymphadeniti In the 15 case of acute ileiti observed by them and operated on they found no intraperitoneal picture that resembled acute mesenteric lymphadenitis either a regard abundant free peritoneal fluid or massive disseminated lymph gland enlargement

In 1932 Strombeck published his ob ervations on 40 cases of acute nontuberculous mesenteric lymphadeniti controlled by operation In 22 in tance he noted the occurrence of acute terminal ileitis which he pre umes was the point of origin of the infection Ten to 20 to 50 cm of terminal ileum proximal to the ileo-cecal valve were involved the intensity of the affection being at the valve and diminishing upward The Peyer s patches were large and grainy boat-shaped swellings The greatest frequency occurred between the ages of 5 and 15 years corresponding to the greatest frequency of acute ileitis Strombeck distinctly states that in the follow up covering at least 4 years he has never seen any such ca e develop into the picture of a chronic regional ileitis Of 31 cases of nontuberculou me enteric lymphadenitis observed by Erskine 10 showed some involvement of the ileum in an inflammatory process associated with large hypertrophied lymph nodes in the me entery He does not relate the disease to true regional ileitis In his opinion the lymph nodes are first involved and then the appendix or the ileum or both by an extension of th process

The observations of Strombeck more or les dispose of the hypothesis that chronic regional enteritis begins a an acute mesenteric lymphadenitis The largest percentage of cases of ileiti in this series were chronic in nature throughout their course The abdominal finding at operation in acute mesenteric lymphadenitis i generalized enlarg ment of mesenteric lymph nodes much clear fluid occasional involvement of terminal ileum In acute ileitis one observes scant free fluid edematous engorgement of

with the lymphatic block The intestinal lymphedema was found to persist as long as ten months without any evidence of subsidence

It is interesting to note that Poppe using similar method of lymphatic injections claims to have produced ulcerative colitis in dogs by obliteration of intestinal lymphatics However Sinaiko and Necheles repeating their work not only failed to produce ulcerating lesion in the colon of dogs but point out in contradiction to the results of Reichert and Mathe that the lesion in the colon showed a tendency to rapid disappearance and no tendency to chronicity Chess et al carried out extensive experiments on 37 dogs and 12 rats using sand and talcum as *sclerosing elements injected into an isolated loop of ileum and cecum* Marked lymphoid hyperplasia of the small bowel was experimentally produced by forced feedings of sand and talc the animals died of plastic peritonitis some of them with granulomas of the liver The intravenous injection of live bacteria in addition to the mechanical effects of the sclerosing substances resulted in ulcerations of both large and small bowel

It had already been suggested (Probstein and Gruenfeld) that normally the flow of the intestinal content is retarded at the ileocecal valve the lymphatic tissue in the mucosa and submucosa is here more abundant than in the segments of the bowel a factor which enhances the likelihood of bacterial absorption Studies on the ileo-cecal junction (ileo-cecus) by Bargen and associates demonstrated longitudinal muscle fibers entering the labia of the valve for a considerable distance and meeting at the crest Gelatin solution injected at the cecal mucosa were blocked at the tip of the labia similar injection made on the ileal side in 15 cadavers were also blocked at the valve Obviously there is a lymphatic blockage at the tip of the labia of the ileocecal junction

Several workers particularly of the English school (Frazer) have considered as an etiological factor some local disturbance in fat metabolism or some fault in intestinal lipoid absorption as being involved in the characteristic tissue reaction of ileitis [1] Hirsch has pointed out that fatty acids in the body produce foreign body giant cell reactions Cooke in his *reflections on steatorrhea and regional ileitis* states To sum up the view is put forward that regional ileitis is the result of tissue reactions to the breakdown products of lipoid complexes or possibly other metabolites or ingested substances leading to further defects in the absorptive powers These may be temporary or persist and aggravate the lesion already present

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the terminal ileum and only localized lymph node involvement Perforation of the acutely inflamed ileum with localized walled off peritonitis is not unusual

Age and Sex in Regional Ileitis

In our series the age distribution at onset of symptoms is shown in table 1

TABLE 1

AGE DISTRIBUTION AT ONSET OF REGIONAL ILEITIS

Years	*Number of Cases*	*Incidence (%)*
1 10	16	3 0%
10 20	130	24 5%
20 30	07	39 0%
30 40	117	? 0%
40 50	37	7 0%
50 60	16	3 0%
60 70	7	1 3%
Total	530	

The average age at onset was 27 6 years The maximum incidence falls between 20 30 years though adolescence is well represented Childhood and old age are scantily represented The oldest case was 74 years of age the youngest case was 9 months in one instance and 2½ years in another The 9 month old case was confirmed by operation and by x ray studies *

TABLE 2

AGE INCIDENCE IN REGIONAL ILEITIS (RAVDIN AND JOHNSTON)

Age Group	*Number of Cases*	*Percentage*
1 10	18	4 7
10 0	68	17 8
20 30	140	36 6
30 40	76	19 9
40 50	40	10 4
50 60	4	6 2
60 70	13	3 4
70 80	3	0 8
Total	382	

* A case of cicatrizing enterocolitis in a newborn has been described in the literature (Kemp Perlongiero and Wein)

These figures compare favorably with those of other authors who have collected a large series of cases Thus *Strombeck collected from* the literature 91 cases the greatest incidence (40 cases) fell between 20 30 years of age or 44 per cent agreeing almost identically with figures in this series Similarly Ravdin and Johnston in a collection of 393 cases from the literature give the age incidence as shown in table 2

At the Mayo Clinic (*Von Patter*) *the age of* patients at *the onset* of symptoms (table 3) of regional enteritis was as follows

TABLE 3

Age at Onset Years	*Patients*
4	2
5 10	21
11 15	62
16 20	103
21 25	116
26 30	113
31 35	66
36 40	34
41 45	37
46 50	21
51 55	11
56 60	4
61 65	6
66 70	1
71 74	3
Total	600

Males predominate over females in their susceptibility to this disease In the present series there are 306 males and 236 females involved representing a proportion of 56 5 per cent males to 43 5 per cent females These figures again agree with the mass compilation of cases from the literature in which males constituted 56 6 per cent of *the cases (Ravdin and Johnston) The figure given in earlier years based* on a smaller group of cases (Crohn) of males predominating over females in a proportion of 2 to 1 is not borne out when large group statistics are invoked

Schiff garnered the statistics from the literature on 48 cases of ileitis in childhood The ages varied from 1¾ *years to 16 years as* shown in table 4

TABLE 4

AGE INCIDENCE OF ILEITIS IN CHILDHOOD (SCHIFF)

Age	Number of Cases
1¾ years	1 case
2 3 years	4 cases
4 6 years	6 cases
7 9 years	18 cases
10 12 years	5 cases
13 14 years	7 cases
15 16 years	7 cases
Total	48 cases

He emphasized particularly the acute phase of the disease in childhood and the similarity of the clinical picture to that of acute mesenteric lymphadenitis

Psychosomatic Factors

Since ulcerative colitis has been generally accepted as one of the so-called psychosomatic diseases the question has been raised Is ileiti also caused by or subject to psychic factors? In the literature the views vary but in general there is little support for such a consideration As early as 1939 Blackburn Hadfield and Hunt studied 22 consecutive cases of ileitis in a control group but could find no psychological characteristics in the ileitis cases Bockus found few phlegmatic individuals in ileitis patients most of them were extremely sensitive and excitable some even manifesting severe psychoneuroses More recently (1951) Dashiel and his group noted some emotional distress in a majority of their 40 cases of ileitis Ingelfinger grouped both ulcerative colitis and ileitis patients as psychiatric problems and economic failures in contrast to the more stable and aggressive peptic ulcer individual Paulley reported 4 cases with unusual dependence Blackburn 4 anxiety states in 22 cases

It is interesting to note that in the large collection of 600 cases reported by Von Patter and his group from the Mayo Clinic no mention is made of psychic factors as influencing the course of the disease Crocket in 16 routine psychiatric examinations of cases of ileitis found no substantial support for the suggestion that emotional stress is a major etiological factor

My own experience does not in any way support the concept of ileitis as a psychosomatic disease The 700 patients we have seen have

been no more no less emotionally unstable than a mass of control individuals When one considers that in the office practice of an internist 80 per cent of the cases seen are functional then the ileitis case by contrast in spite of his severe organic symptoms seems temperamentally quite stable True many cases of ileitis have been rescued from psychiatric institutions but that is only because the diarrhea was regarded as nervous and the true source of the illness was completely missed The debilitating effects of the organic symptoms and the associated anxiety eventually break down the most complete self-control The older age groups of ileitis cases are remarkable for their fortitude and stamina in spite of low grade symptoms covering long periods of years nor is there anything to approach the ebullience and self sufficiency of a healed case of ileitis (postoperative) even though a recurrence of his illness catches up with him 19 or 25 years later Among the 500 cases recorded in Canadian hospital in a recent five year period (Turner) many of the cases were farmers and urbanites no particular category of personalitie could be discerned

We know of no single illustrative case where the onset of ileitis was associated with or could be attributed to psychic traumatic situations Nor can we attribute recurrences of the disease postoperatively to any psychic factors Many recurrences take place 11 14 17 19 or even 25 years after the original operation and it is difficult to conceive a former patient who survived the vicissitudes of life over all those years falling prey to a recurrence of ileitis merely as a result of a more unusual set of adverse psychic factors

An interesting instance of both psychic strain and physical disease as the background for the etiology of regional ileitis is seen in the following case

H B Serial No 20 male age 29 years Patient enlisted in the U S Army in 1939 serving in the Philippine Islands He was a prisoner of war from 1942 to 1945 one of the many who participated in the Death March from Corregidor He suffered from bacillary dysentery amebic dysentery undulant fever malaria pellagra scurvy beri beri and severe malnutrition During all this time he had severe diarrhea In July 1945 the diagnosis of regional ileitis was made by x ray examination the granulomatous process involving the whole of the ileum When seen in 1946 he had recovered weight and strength and was well except for the diarrhea X ray examination demonstrated a normal colon but a severe diffuse regional ileitis The sigmoidoscopy was negative

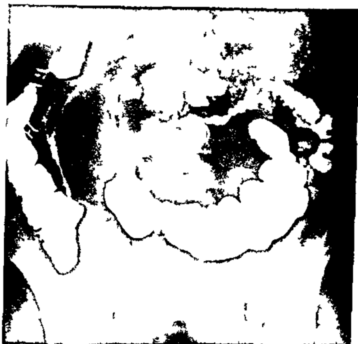


FIG 3 *Regional ileitis in a man who survived the Death March and three years in a Japanese concentration camp*

Social Status Race Nationality Religion

All classes of society are affected equally by ileitis private hospitals and public wards seem equally represented in proportion to population Bockus appears impressed with the failure to encounter regional ileitis in families who have been in the upper economic brackets for one or two generations All races and climes seem represented in this disease since the literature from all over the world contains publications of cases (Africa India Sweden Puerto Rico East Africa South America) Bockus again mentions the fact that no cases had been reported from Latin America or from Cuba this deficiency has since been supplied (Fermin also Valencia Parpacen) He also observed a paucity of cases from the southern sections of South America In 1944 there were 134 admissions from ileitis in the total U S Army in 1945 there were 145 similar admissions for the entire Army The corresponding rate per

1000 strength for each year is 02* Kiefer found that regional ileitis occurred 70 times in 100 000 registrants at the Lahey Clinic

As regards race a greater incidence of the disease among the Jewi h race was fir t suggested by Homans and Hass In the experience of Bockus 13 of 21 cases were Jewish thrice the normal expectancy of the disease for the sample from which the cases were drawn However in Marshall s series at the Lahey Clinic only 3 of 29 cases were Jews Ashley at the Harper Hospital in Detroit found only 8 of 31 cases in his series to be Jews Brown and Donald 26 per cent Jews (Mayo Clinic) The study compri ing 22 ca es of ileitis in the records of the Binghamton City Hospital and other ho pitals in Broome County New York include no cases involving Jewish patients (Sneirson and Ryan) Negroes Orientals and Latin Americans are all represented and reported in the literature one of my own cases was a Hindu from British India Strombeck of Stockholm with 26 cases reported and with an extremely careful analysis of etiology fails to mention race or social position

* Personal comm n cat on

Chapter 3 Gross Pathology

Gross Pathology

REGIONAL ILEITIS is a nonspecific granulomatous inflammation of the ileum involving most frequently the terminal segment or segments of the small bowel In gross appearance it has definite characteristics that distinguish it from granulomata elsewhere in the alimentary tract these specific features being most pathognomonic when the terminal ileum alone is involved The histologic microscopy of the disease is nonspecific it is not to be differentiated from other granulomata from sarcoid and (often only with difficulty) from tuberculosis

In our series of 542 cases the extent of ileal invasion was noted in our records in 511 instances The inability to state the amount of anatomic involvement in the remaining cases was due to the fact either that they had been previously operated on elsewhere or that no surgical corroboration of the radiographic picture had been obtained

The anatomic distribution in this series is shown in table 5

TABLE 5

ANATOMIC DISTRIBUTION IN REGIONAL ILEITIS (FIG 3)

Distal (inches)		*Cases*
12		222
24		167
2 3	(feet)	55
3 4	(feet)	13
4 6	(feet)	47
Mid ileum		7
	Total	511

In one remaining case the terminal ileum and the uppermost ileum were discontinuously involved The predominance of the lesion limited to the terminal 12 inches of ileum is noteworthy the next longest group not only involves the terminal segment but extend continuously to cover the distal 24 inches of ileum the smallest group involves the terminal and all of the upper reaches of the ileum which we arbitrarily indicate as being about 6 to 7 feet in length from the ileo cecal valve

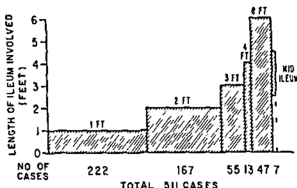


FIG 4 Anatomic distribution of pathol gic lesion (cases) ileo cecal valve to trans t on between ileum and jejunum

In the series reported by Blackburn Hadfield and Hunt of 22 cases the terminal ileum was involved in 19 instances the distal ileum in 3 instance In 6 cases the cecum was involved in an analogous extension of the proce s The length of ileum involved varied between 4 and 60 cm with an average of 19 cm (7½ inches)

Why the terminal ileum is so often the sole seat of the disease and apparently the oldest and parent lesion in the process is difficult to explain Mo t general diseases of the small bowel are located at or near the terminal ileum just proximal to the ileo-cecal valve These include benign and malignant new growths foreign body granulomata primary and secondary hyperplastic tuberculosi sarcoid carcinoid and endometri osis The normal narrowing of the lumen of the small bowel as it progresses di tally is maximum ju t proximal to the valve of Bauhin the valve itself con titutes a mechanical device for slowing up the progress of the column of chyme the lymphatics of the intestinal wall particularly the mesenteric lymph nodes are in their greatest density at or about the ileo cecal angle The natural blockage of the lymphatic drainage at the labia of the valves as shown by Bargen et al localizes an infection proximal to the valve and di courages or prevents in the largest per centage of ca e the transition or extension of the disease to the cecum Occasional cases are cited where the lesion involves a very short segment of ileum proximal to the valve without involving the actual terminal segment of the ileum but the e cases are exceedingly rare

The gross appearance of ileitis as seen at the operating table

Chapter 3 Gross Pathology

Gross Pathology

REGIONAL ILEITIS is a *nonspecific granulomatous inflammation of the ileum involving most frequently the terminal segment or segments of the small bowel In gross appearance it has definite characteristics that distinguish it from granulomata elsewhere in the alimentary tract these specific features being most pathognomonic when the terminal ileum alone is involved The histologic microscopy of the disease is nonspecific it is not to be differentiated from other granulomata from sarcoid and (often only with difficulty) from tuberculosis*

In our series of 542 cases the extent of ileal invasion was noted in our records in 511 instances The inability to state the amount of anatomic involvement in the remaining cases was due to the fact either that they had been previously operated on elsewhere or that no surgical corroboration of the radiographic picture had been obtained

The anatomic distribution in this series is shown in table 5

TABLE 5

ANATOMIC DISTRIBUTION IN REGIONAL ILEITIS (FIG 3)

Distal (inches)			*Cases*
1			[illegible]
24			167
2 3	(feet)		55
3 4	(feet)		13
4 6	(feet)		47
Mid ileum			7
		Total	511

In one remaining case the terminal ileum and the uppermost ileum were discontinuously involved The predominance of the lesion limited to the terminal 12 inches of ileum is noteworthy the next longest group not only involves the terminal segment but extends continuously to cover the distal 24 inches of ileum the smallest group involves the terminal and all of the upper reaches of the ileum which we arbitrarily indicate as being about 6 to 7 feet in length from the ileo cecal valve

to separate the loops it will frequently be noted that they are adherent because of fistulous communications or fistulous tracts originating in the porous terminal ileum extending through the mesentery to the adjoining loops of small or of large bowel Occasionally a slow walled off perforation of the terminal loop of ileum will be observed covered over by a plastic exudate and sealed off by neighboring viscera usually another loop of ileum or the sigmoid Bockus emphasizes that there is a close relationship between the destructive changes in the mucosa and the extent of covering of the serosa with mesenteric fat The termination of the mesenteric fat on the antimesenteric portion of the serosa corresponds to the line of demarcation between diseased and normal mucosa

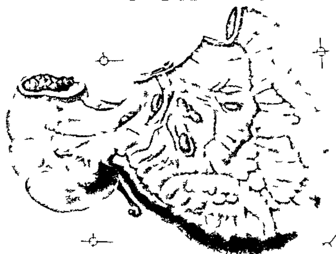


Fig 6 Characteristic appearance of lesion in regional ileitis involving terminal ileum and segmental lymph nodes

After the resected specimen is opened one notes the edema and thickening of all the coats of the bowel (figs 5 6) The lumen of the bowel itself is reduced and compromised by the swelling of the walls until the actual lumen is reduced to a cordlike stenotic opening This reduction of the lumen of the bowel in old chronic distal ileitis accounts for the characteristic string sign seen in radiographic films The process may continue to true stenosis with intestinal obstruction and proximal

or as studied in the resected specimen is that of a brilliantly red congested edematous mass—solid and firm resembling a rubber hose or as Dalziel has described it an eel in a state of rigor mortis' An equally apt description is that of Jackson who likened the diseased segment to a dead water soaked night crawler' The serosal surface is *greatly injected usually covered by fibrinous exudate the lumen of the* gut may be dilated or in the end stages reduced to a narrowed cordlike tube The extent of involvement is manifest by the varying degrees of hyperemia the engorgement of the vessels the serosal exudate and the gross enlargement of the accompanying mesenteric lymph nodes The hyperplasia of the mesenteric lymph nodes parallel the extent and degree of the inflammatory lesion Where the lesion ends usually more or less abruptly the serosa of the proximal bowel appears normally shiny and smooth and the obviously enlarged mesenteric nodes are no longer visible

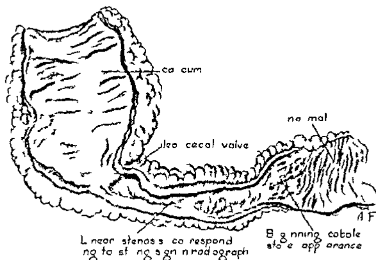


Fig 5 Characteristic lesion in resected specimen typical regional (terminal) ileitis basis of string sign

The mesentery of the involved bowel is boggy swollen and visibly thickened Usually one or more loops of small intestine are matted together forming a palpable inflammatory mass If an attempt is made

tion on a pathologic basis seems amply verifiable The first or localized group may and does progress to stenotic fibrosis remains stationary and may lead to intestinal obstruction They lend themselves favorably to surgery The second group is scattered progressive in the nature of a mucosal or submucosal lesion less well defined anatomically with less involvement of regional lymph nodes and less amenable to accurate definition during exploratory operation This mucosal or submucosal type explains to a large degree the disappointing end results of surgical intervention

Microscopic Pathology

There are no specific features that characterize or are pathognomonic of ileitis in contrast to granulomata or so-called pseudotuberculous diseases in general The histologic sections show varying degrees of acute subacute and chronic inflammation predominantly marked by infiltration of polymorphonuclear leukocytes plasma and round cells and fibroplastic elements The earliest lesion is apparent in the submucosa where the intensity of the lesion is greatest (Hadfield Schepers) Several observers have agreed in regarding the submucosa as the original site of the onset of the disease process The more superficial necrosis and ulceration of the mucosa is the result of inflammatory arteritis and phlebitis of the underlying vascular supply The mucosa is desquamated the architectural structure of the glandular tissue is destroyed and replaced by plasma and round cell infiltration In the late stages of the disease the inflammatory reaction is more focal in character covered on the mucosal side by nodular thickening reminiscent of tubercles The enlarged congested skeins of inflamed lymphatics are often apparent even through the thickened serous peritoneal covering Mallory made much point of the fact that he found large and numerous endothelial leukocytes lying free and blocking the lymph spaces as well as lying in the interstitial tissues These cells are flat and polygonal with granular eosinophilic cytoplasm and hyperchromatic nuclei The reaction is sharply focal and intervening stretches of the lymphatics show dilation These same findings have been confirmed by the histologic studies of Rappaport Burgoyne and Smetana

Microscopically the presence of giant cell is very striking In the vicinity of the giant cells one often sees groups of pale cellular structures resembling vegetable cells in nature The giant cells are not specific to ileitis they had been noticed previously by Moschcowitz and Wilensky

dilatation of the bowel loops the stenosis being due to cicatricial contraction of old inflammatory scar tissue at the site of the ulcerating lesions

The mucous membrane has a cobblestone appearance due to the fact that the transverse folds of the mucosa are in part destroyed and are intersected by deeply grooved longitudinal ulcerations that extend through the length of the specimen These longitudinal ulcerations are deepest along the mesenteric border of attachment it is in this area along the mesentery that the sinus and fistula tracts emanate The surface of the mucosa is superficially desquamated the markings are gone deep ulcers 0 5 cm to 1 cm in diameter are interspersed between areas of proliferated almost polypoid hyperplastic mucosa True polypoid formation in late cases as seen in ulcerative colitis is frequently observed The submucosa is markedly thickened edematous and congested the muscularis is thickened and hyperplastic the serosa its sheen gone is bright red many times its normal thickness in depth and covered by *exudate (Otani)*

The gross lesion in the bowel wall terminates rather abruptly a sharp line of demarcation is lacking but the mucosa within one or two inches of the proximal area of involvement will suddenly lose its edema and thickening and shortly resolve into normal mucosa Unfortunately the inflammatory process has a tendency to extend proximately by kangaroo like jumps skip lesions of involvement are common proximal to the distal involved segment these skip lesions being separated by skip areas of normal mucosa The extent of the skip may vary from a few inches or in multiple skip lesions to several inches up to 2½ feet between the parent and the skip lesion Occasionally one sees isolated skip lesions from terminal ileum to mid jejunum and even to duodenum itself

In older phases of the disease the exudative or inflammatory reaction is replaced by a fibrostenotic process the mucosa appears atrophic with occasional superficial erosions and islands of papillary or polypoid hyperplasia The lumen of the gut may be so reduced as barely to admit a large probe In advanced cases extensive inflammatory polypoid formation is visibly evident and is readily demonstrated by radiography

Pemberton and Brown have made an important contribution in differentiating the lesion in ileitis into two categories (1) involvement of a shorter or localized segment of the ileum a single lesion (2) a similar process which involves large segments usually multiple with a greater tendency to progressive extension Clinically this differentia

tion on a pathologic basis seems amply verifiable The first or localized group may and does progress to stenotic fibrosis remains stationary and may lead to intestinal ob truction They lend themselves favorably to surgery The second group is scattered progressive in the nature of a mucosal or submucosal lesion less well defined anatomically with less involvement of regional lymph nodes and less amenable to accurate definition during exploratory operation This mucosal or submucosal type explains to a large degree the disappointing end results of surgical intervention

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FIG 7 Pseudo tubercle with epitheliod cells arranged in a whorl around giant cells in submucosa (Regional ileitis)

in their study of intestinal granulomas and were thought by them and by subsequent writers to be due to foreign body inclusions vegetable matter or lycopodium spores Homans and Hass thought the giant cell to be a reaction to lipoid material Reichert and Mathes to possible silica or talc inclusions This vegetable material becomes entrapped in the deep mucosal ulcerations enters the lymphatics and becomes encapsulated in the process of healing The attempts of earlier authors to include ileitis as a form of tuberculosis was probably due to the findings of giant cells of the Langerhans type Warren and Sommers were able to reproduce the disease by sclerosing substances and by the injection of lipid materials They also observed that two specimens removed from cases of regional ileitis contained colorless rounded objects with smooth surfaces They were doubly refractory and polarized light

Hadfield has made an intensive histologic study of 20 resected specimens at St Bartholomew s Hospital in London He particularly emphasized the early and intense involvement of the submucosa considering that the mucosa was probably secondarily involved in the process of extension and also by necrosis due to vascular infiltration The early



FIG 8 Lymph node sh wing pseud tubercle format on with g ant cell system

changes in the submuco a consi t of hyperpla ia of the lymphatic tissue and obstructive lymphedema The submucosal hyperplasia and early and extensive involvement of the lymphatics occurs in his experience in 95 per cent of the cases These early area of lymphadenoid tissue show clear evidence of cellular activity with a central zone of proliferating reticulum cells surrounded by a narrow zone of lymphocytes (figs 8 9) A specific respon e occurs The affected germinal centers become re placed by proliferating endothelial cells A Langerhans giant cell can usually be found at the center of the nodule The follicle now becomes a giant cell system Hadfield states that in the several hundred sections he has examined caseation has never been observed The typical specific reaction with giant cell inclusions characterized the sections of lymph nodes found in the mesentery and accompanying the specific lesion in the gut (figs 9 10)

Actually Hadfield found giant cells in 13 out of 20 cases examined Necrosis within the granulomatous areas in the ileum or in the lymph nodes rarely occurs caseation never In the series of Warren and Sommers necrosis was observed in 8 of 61 cases (13 per cent) Refer

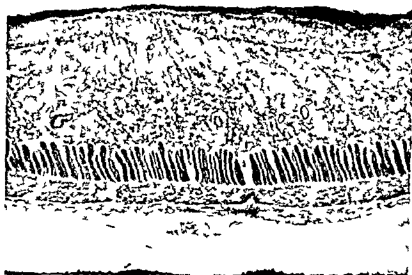


FIG 9 Longitudinal section of kip lesion Marked submucosal thi kening d e to granulomatous infiltration Epithelium completely ul erated and surface covered with a prurulent exudate

ence has been made to the case of Frazer and Haggar in which caseat *ing tuberculous mesenteric lymph nodes were observed in the resected* specimen though the ileiti proper was nonspecific in origin

Endarteritis obliterans and perivascular infiltration with collections of plasma cells were emphasized by Binney Early involvement of nerve tissue particularly Auerbach plexus was noted by Barbour and Stokes though these changes are not specific They even suggested that a chronic recurring intussu ception might initiate the process by impairing the circulation and vitality of the gut wall Schepers divides the lesion into two component a primary phase characterized by (a) a stage of edema of the submuco a and the ero e with dilatation of submucosal lymphatics and hyperemia of juxtamuscular adventitial blood ves els (b) plasma cell infiltration of submucosa and serosa (c) diffuse fibrosis with disappearance of plasma cell (d) healing a secondary phase character *ized by ulceration of the muco a and submucosa which is superimposed* on the primary pha e with eventual tendencies to late or early perfora tion fi tulation and granuloma formation



Fig 10 Cross section of chronic terminal ileitis showing stenosis of the lumen caused by extensive granulomatous infiltration of the submucosa

There are two more recent thought provoking observations on the pathology of ileitis In resected specimens Brunner like glands have been observed in the mucosa and in the submucosa in cases of ileitis These glands are similar to those appearing in the normal histology of the duodenum and the pylorus [7] Sixteen of 34 such resected specimens show on microscopic study such Brunner like glands most of these cases were later shown to be followed by recurrent disease (Kawel and Tesluk)

Davis Dockerty and Mayo made comparative studies of the number of ganglion cells in the myenteric plexuses of the normal bowel as compared to those of regional ileitis [8] Persons suffering from regional enteritis possess in the mesenteric plexuses of the small intestine approximately three times as many ganglion cells as persons not so afflicted Regional enteritis of long duration is attended by a greater increase in ganglion cell count than diseases of short duration

In both these observations the changes observed may be secondary rather than primary in nature as a causative agent in the disease

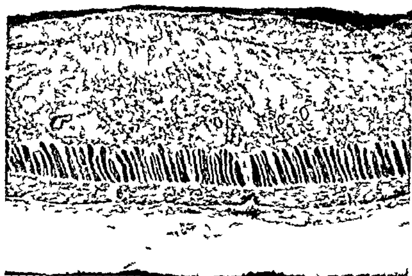


FIG 9 Longitudinal section of skip lesion Marked submucosal thickening due to granulomatous infiltration Epithelium completely ulcerated and surface covered with a prurulent exudate

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next largest group falls between 5 and 20 years before recognition of the disease The one with a 50 year unrecognized diagnosi was a Hindu from British India Blackburn states that the average duration of symptoms before operation was 31½ month Clark and Dixon found that the average duration of symptoms before observation wa 4 1 years the longest duration of symptoms 25 years

If one were to speak of prodroma one could mention only the suppurative rectal complications which so often precede by years the onset of manifest symptoms The e rectal or perirectal abscesses and fistulas occurred in 86 of 542 cases the real significance lies in the fact that they so often precede the on et of diarrhea If they do not actually antedate the diarrhea they are so obvious and the diarrhea so minimal that to most uninitiated observers only the fi tula or perirectal abscess exists On one occasion a patient who was admitted to the ward for routine hemorrhoidectomy was observed to have a small rectal fistula A resident physician detected a vague hi tory of diarrhea and asked for radiographic study which disclo ed a terminal ileitis

The one other phenomenon that stigmatizes the onset of ileiti is the scar of a previous appendectomy This scar was evident in 116 or 21 4 per cent of our series of cases and was a signal of previous abdominal pain localized in the lower right quadrant of the abdomen Ravdin and Johnston in a review of cases published in the literature found that a previous appendectomy had been performed in 27 1 per cent of the cases The diarrhea which characterizes most of the cases of ileitis was undoubtedly overlooked the abdomen was opened an innocent appendix removed and the ileitis not observed

The onset of the true symptoms of ileitis or enteriti is characterized when typical by the initiation of diarrhea abdominal pain low grade fever progressive anemia and lo s of weight and eventually by the ability of the clinician to feel an intra abdominal mas *Diarrhea* wa present in 491 of the 542 cases of regional ileitis The diarrhea is an outstanding feature of the disease though in number of movements and in intensity it rarely approaches that of ulcerative colitis The rule that frequency of fecal movements in an inflammatory intestinal process i in inverse proportion to the di tan e from the anal sphincter hold good *Ulcerative* proctiti gives usually *10* to *20* stools a day with urgency tenesmus and the appearance of fresh blood in the stool Ulcer*ative colitis in the distal* colon may average 5 10 stool a day right sided or segmental colitis is notable for lessened frequency of defecation

Chapter 4 Clinical Features

Onset

THE USUAL CASE of regional ileitis does not begin as an acute and sudden manifestation its onset is usually hidden in the deep past with such intervening symptoms as an occasional spell of diarrhea a progressive malaise or nervousness often verging on true psychoneurosis A rectal suppurative complication may long precede the manifest initiations of diarrhea Gradually the diarrhea increases in severity and is now accompanied by abdominal pain low grade fever is occasionally noted with loss of weight In the prodromal stages the patient loses little efficiency or time from his work or occupation The progressive symptoms build up over the course of years to the finally fully developed picture of regional ileitis Such is the most common picture of the onset Some unusual forms of onset have been noted in this series e g initial intestinal obstruction 4 cases onset with hematemesis and melaena 2 cases onset with dysuria one case onset with sealed off perforation one case

The duration of symptoms before the actual recognition and diagnosis of the disease in this series may be seen in table 6

TABLE 6

DURATION OF SYMPTOMS BEFORE RECOGNITION OF REGIONAL ILEITIS

Duration	*No of Cases*
0 6 months	0
6 12	37
1 2 year	86
3	78
3 5	86
5 10	96
10 15	47
15 20	34
20 30	15
30 40	1
40 50	
Total	482

It will be seen that the largest group of cases falls between one and 5 years duration of symptoms before the initiation of therapy the

of the ileum that segment which radiographically corresponds to the string-sign The attempt of the intestinal fluid column to pass through this congested edematous and narrowed stretch of intestinal lumen gives rise to the colicky sensation of pain The absence of pain occurs in those cases in which the inflammatory lesion i diffuse the mucosal type in which the beginning cicatricial process is still young the mucosal pattern is altered by the stenosing string-sign the quill like narrowing has not yet supervened The higher the process in the ileum the less likely the stenosis and hence the less likely predefecatory pain In the late long standing case where true stenosis supervenes the pain is of course severe and sharply colicky Occasionally primary intestinal ob truction characterizes the onset of regional ileitis or at least its symptomatic phase

Nausea and vomiting are rare manifestation and occur only in the later stenotic phase of the disease Appetite is usually well preserved in contrast to ulcerative colitis where loss of appetite absolute anorexia and even vomiting are common manifestations and parallel the intensity of the toxic process Ulcerative colitis is a much more toxic disease than regional ileitis and the interference with appetite and with nourishment is in contrast to the milder manifestations and retained desire for food which i present in ileitis

Fever occurred in roughly one third of the cases in this series The fever is of the low grade type the temperature usually normal in the morning ri es to 100 5 degrees 101 degrees or rarely 102 degrees F in the late afternoon It is irregular in type though often persisting it i not accompanied by chills or sweats Many if not most of the cases are afrebrile throughout The fever characterizes the acute or inflammatory phases of the proces the intervening stages of remission are afebrile the late cicatrizing phase of the disease is also afebrile

The continuous low grade fever of ileitis like that of segmental or right ided colitis is frequently mistaken where the diarrhea is minimal and unnoticed for many of the other di eases which are also characterized by low grade fever and low leukocyte counts in the circulating blood In 11 cases in this series the onset of the disease was characterized by fever of unknown origin as the fir t and presenting symptom Undulant fever brucellosis subacute bacterial endocarditis and lupus erythematosi disseminatus are frequently the connotations given to the low grade febrile type of ileitis without any noticeable diarrhea or abdominal pain

perhaps 3 6 per day Regional ileitis with all its pathologic process proximal to the ileo-cecal valve is noted for mild diarrhea 2 to 4 or 5 movements in 24 hours

Each individual movement is usually preceded by a spasm of abdominal pain The characteristic sequence of events is similar to Moynihan s classic description regarding duodenal ulcer— pain food relief pain In ileitis the sequence is abdominal pain or colic desire to defecate the feeling of sudden rumbling of gas followed by defeca tion with relief of all subjective abdominal symptoms—so called pre defecation pain This sequence may repeat itself every few hours of the day less at night it is often initiated by the taking of a meal The defecations are not urgent or spurting in nature The stool is mushy semi formed or liquid it contains some excess of fluid mucus but never evident pus and only rarely blood In fact occult bleeding in the stool on examination with guaiac is usually negative The stool may be slightly acid or alkaline or it may be neutral the reaction here has no significance

Either a normal number of daily movements or constipation (49 cases) mark the remainder of this series Not infrequently even in a mature case of ileitis no history of diarrhea is obtainable and in some few cases actual constipation was noted The presence of constipation does not necessarily denote obstruction since only in the late phases of intestinal obstruction is the constipation acute and obdurate In those cases in which constipation has been present the remaining symptoms of abdominal pain colic a mass and a progressive course have also been negligible the radiographic study establishes the diagnosis

Abdominal pain was noted in practically all instances in this series This fact is not surprising for pain in the abdomen seems so constant a complaint in the anamnesis that one would expect its presence in almost all of the cases The pain is usually mildly colicky in nature most often situated in the lower abdomen preferring the right lower quadrant or the suprapubic region as its site Occasionally the pain is solely in the left lower quadrant and in a few cases covers the whole lower and upper abdominal segments The pain precedes and is relieved by defecation When the inflammatory mass becomes adherent to the sigmoid loop of colon and pinned down to that viscus by internal fistulas the pain and the mas are likely to be localized in the left lower rather than the right lower quadrant of the abdomen

The origin of the pain is in the mildly obstructive narrowed loop

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The leukocyte count in the circulating blood in ileitis is not usually materially elevated The range may be between 9 000 and 12 000 white blood cells rarely higher A shift to the left of the polymorphonuclear leukocytes and toxic granulations is rarely seen in contrast to severe ulcerative colitis where both these conditions are frequent Eosinophilia as in ulcerative colitis is common the rate rising to 4 to 8 to 12 per cent in a small number of cases The explanation of the eosinophilia in both conditions is not apparent The attempt to explain the eosinophilia on an allergic basis is not satisfactory nor are foreign body inclusions a reasonable answer The eosinophilia is part of the general systemic reaction to the disease In acute ileitis the total white count is higher and a greater percentage of polymorphonuclear leukocytes is present in the circulating blood a fact that only intensifies the confusion in differentiating acute ileitis from acute appendicitis An increased sedimentation rate of the red blood cells is usually observed according to Snapper Pompen and Groen

A moderate often progressive anemia characterizes regional ileitis In advancing cases the hemoglobin reading may range from between 60 per cent and 70 per cent on the Sahli scale lower readings are not unusual even in the absence of gross intestinal hemorrhage In one case in this series the hemoglobin fell to 32 per cent Sahli without evidence of melaena In another case twice operated on for recurrent ileitis the severe anemia of 16 per cent hemoglobin was explained when the true picture of a primary pernicious anemia became apparent in the blood smears An achylia gastrica was present reticulocyte response to liver extract absent in this individual The pernicious anemia in this case was incidental and probably not related to the regional and recurrent ileitis

Gastric secretory changes in ileitis are unusual One regularly notes a normal type of curve in the fractional test meal the secretory curve may however be low (hypoacidity) Apart from the above cited case complicated by pernicious anemia only once was true achylia gastrica seen in this series

The *general symptoms* of ileitis are those of weakness loss of strength and loss of weight A material weight loss was noted in 143 cases in this series in one instance the loss amounted to 50 pounds In the advanced cases those with intestinal obstruction and following debilitating operation the loss of flesh may be much greater and more extreme in terminal case amounting to emaciation This extreme is

however unu ual The average ca e may lose 10 15 or 20 pounds the patient find it difficult to regain weight because of the persistent diarrhea and abdominal pain Following successful operative procedure the regain of weight is rapid and ample The lo s of strength is not extreme many patients with mild ileiti are able to continue at their work with little loss of efficiency In one in tance a man in the Armed Forces during the Second World War was able to continue in active service for 3 years after the onset of diarrhea which signalized the initiation of the ileiti the diagnosis then being unrecognizable or unrecognized In a man 71 years of age who complained of anorexia weakness moderate diarrhea and a lo s of 25 pounds of weight simulating cachexia the entire clinical picture was one of ma ked carcinomatosis Repeated x ray examinations of the gastrointestinal tract were reported as negative Eventually exploratory operation revealed a regional ileiti involving 60 cm (24 inches) of terminal ileum

Retarded growth and delayed secondary sexual maturation in children was occasionally noted in this series of regional ileitis Where the higher reaches of the ileum and the j junum are involved the interference with growth and maturity will be ob erved to be much higher

Men truation is u ually regular and maintained in contra t to ulcerative colitis where amenorrhea characterized the more severely toxic nature of that disease

Joint pains were pre ent in 17 cases in thi series the larger joints such as ankle knee and elbow being u ually involved as is so commonly seen in segmental colitis The small joints of the hands and feet are spared in ileitis Clubbing of the fingers of the hand occurred 22 times in thi series Erythema nodosum was observed 7 times usually but not always associated with arthritis

The nervous or rather psychic manifestations of this disease are sometimes so manifest that they overwhelm the true somatic manifesta tions This occurred in 18 cases in this series that we know of probably much more often In 6 of the ca es the on et of symptoms occurred while the patients were in active service in the Armed Forces Most of the ca e were regarded as psychoneurotic following exposure to battle or due to bomb shock some were classed as nervous diarrhea or as food poi oning In civilian life 10 case were treated a depressions or as neurasthenia 8 of them in institutions for mental care The evident psychic and nervous ymptoms that accompany ileitis often lead to

delayed recognition of the true causes for the symptoms Of Blackburn s 22 cases one suffered from a true psychosis and 4 were referred to psychiatrists for mental treatment when as he states a routine clinical pathological and radiological investigation would undoubtedly have shown organic disease of the ileum

However ileitis can hardly be classed as a psychosomatic disease occurrences or recurrences do not follow upon psychic shock as evidently as they can be ob erved in ulcerative colitis with relationship of cause to effect

Physical Examination

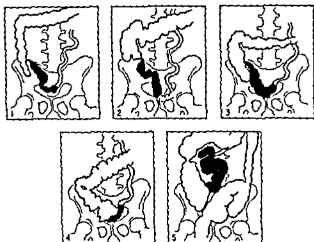
The two outstanding features in the physical examination of the cases of regional ileitis are (1) an abdominal mass and (2) evidence of fistula formation external and internal

The abdominal mass (observed in 185 cases in this series) is usually found in the right lower quadrant of the abdomen in an anatomic area corresponding to the inner surface of the cecum The mass varies in size from that of a finger to that of a lemon a large orange or occasionally even larger The mass is usually fixed to the posterior wall to the cecum or to the anterior abdominal wall particularly when an external fistula is present leading anteriorly from the mass Tenderness on palpation is constantly present when the mass is small and in its typical site it is with difficulty differentiated from a spastic cecum The mas consists materially of the inflamed terminal loop of ileum and of adherent loop of nearby ileum or of cecum ascending colon or sigmoid

When the segments of the mass are separated at the operating table it will usually be seen that the intestinal loops are adherent because of single or multiple intercommunicating fistulous tracts The mass particularly when adherent to the dome of the urinary bladder may be apparent in the lower midabdomen in one instance simulating a urachus cyst In another in tance the loops of ileum were adherent to and drawn over by the sigmoid colon the ma s being palpable to the left of the midline of the abdomen

The most common seat for the mass i low in the right lower quadrant of the abdomen palpable frequently by rectal or vaginal pelvic examination or by bimanual technic Thi fact is easily explainable the position of the terminal ileum is dependent from the cecum Testut places the cecum below the pelvic inlet in 15 per cent of males and in 30 per cent of female bodies In the upright position the cecum and loops of

terminal ileum fall into the pouch of Douglas in the female and between the bladder and rectum in the male Very often these loops lie directly



NORMAL TERMINAL ILEUM
VARIATIONS IN ANATOMICAL POSITIONS

Fig. 11 Anatomic pos t on of the normal terminal ileum
(1) Usual posit n of c cum and leum (2) High cecum ile m descent to pelv s (3) Lo v cecum medial implantation of ileum (4) Complete descent cecum and ile n in pelvis (5) Except onal p ition ileum in abrupt a cent

on the pelv floor (fig 11) upported by the levator ani muscle Monks found the terminal ileum to be in the pelvis in more than 50 per cent of his studies In our own radiographic stud es made to deter mine the position of the normal ileum it was found (Crohn and Yarnis) that in 150 control normal cases descent of the cecum and terminal ileum into the lower pelvis occurred in 28 per cent of the observed cases in that eries In the pathologic ileum (25 cases of terminal ileitis) the terminal affected loop of ileum wa found in the pelvis in all cases—in fact on the floor of the pelvic cavity (fig 12) It is apparent that the soggy weighted diseased ileum descend low down in the righ lower abdominal quadrant and being even heavier than normal in weight occupies almost uniformly the pelvic inlet The mass of ileitis i then found and easily palpated by bimanual technic in the fossa of Douglas Only when adher ence to other organ takes place is the mass felt other than in the right

delayed recognition of the true causes for the symptoms Of Blackburn s 22 cases one suffered from a true psychosis and 4 were referred to psychiatrists for mental treatment when as he states a routine clinical pathological and radiological investigation would undoubtedly have shown organic disease of the ileum

However ileitis can hardly be classed as a psychosomatic disease occurrences or recurrences do not follow upon psychic shock as evidently as they can be observed in ulcerative colitis with relationship of cause to effect

Physical Examination

The two outstanding features in the physical examination of the cases of regional ileitis are (1) an abdominal mass and (2) evidence of fistula formation external and internal

The abdominal mass (observed in 185 cases in this series) is usually found in the right lower quadrant of the abdomen in an anatomic area corresponding to the inner surface of the cecum The mass varies in size from that of a finger to that of a lemon a large orange or occasionally even larger The mass is usually fixed to the posterior wall to the cecum or to the anterior abdominal wall particularly when an external fistula is present leading anteriorly from the mass Tenderness on palpation is constantly present when the mass is small and in its typical site it is with difficulty differentiated from a spastic cecum The mass consists materially of the inflamed terminal loop of ileum and of adherent loop of nearby ileum or of cecum ascending colon or sigmoid

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festations indicate the degree of general body affection a part of the localized intestinal process

Erythema nodo um on the anterior a pect of the lower extremities was noted once in acute ileitis and 6 times in chronic regional ileitis This phenomenon which is so much more prevalent in ulcerative coliti po ibly links the two di eases in a common etiologic factor

Obstructive Phenomena

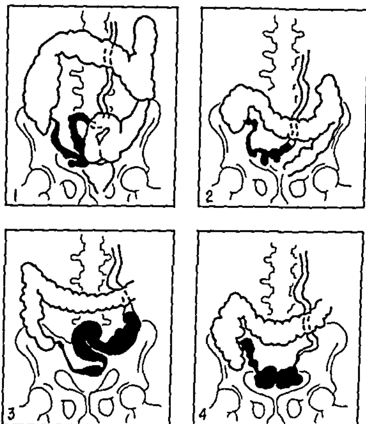
Intestinal obstruction occurred in 45 instances in thi eries of 542 cases usually late in the course of the disease Four times in the series it was an early—in fact the presenting—symptom at the onset in the other cases it indicated a long standing chronic inflammatory process eventuating in chronic cicatricial steno is of the bowel at the site of the lesion Sherill and Hall indicate two cases with obstruction as the initial phenomenon though both were old chronic ca es Jackman reported two cases of hypertrophic enteritis as a cau e of intestinal ob truc tion—both of the acute type—in which the terminal ileum was perforated during the operative manipulations

Occasionally the obstruction may be due to angulation and kinking of a loop of bowel by peritoneal adherence or by ileo ileal fistulation Loops of di tended intestine may be seen through the thin abdominal wall visible peristal is i not uncommon and is accompanied by severe abdominal cramps and borborygmi A scout film of the abdomen will show puddling and fluid level Vomiting may be present in the more severe stenotic phases The obstruction can usually be temporarily alleviated by the use of the Miller Abbott or Harris tube

Postoperative intestinal obstruction such as characterizes many cases of intestinal resection or short-circuiting operations is unfortunately only too frequent but happily doe not occur as frequently as in recon structive surgery for ulcerative colitis

Pancreatic Insufficiency in Regional Ileitis

It i interesting to note that both in regional ileitis and in ileo jejunitis Dreiling found evidence of pancreatic insufficiency in a fair percentage of uch ca e By mean of the secretion test he demonstrated low maximum HCO3 concentrations in three in tances and low total amylase estimation in 5 out of 22 subject submitted to the te t A moderate degree of pathologic change namely fibrosis ha al o been reported



VARIATIONS IN ANATOMICAL POSITIONS OF ILEUM IN TERMINAL ILEITIS

Fig. 14. Anatomic position of diseased ileum. The weight of the diseased ileum carried it downward to lie in the pelvic floor.

lower abdominal cavity. When fistulous tracts burrow into and through the apposed base of the mesentery, the necrotic process may cause a diffuse suppurative mesenteritis, which participates in and increases the size of the inflammatory mass.

Apart from the abdominal mass and the demonstration of characteristic fistulas, the physical examination of the cases of ileitis is likely to be negative. Enlargement of the spleen was noted 6 times; clubbing of the fingers 22 times, not necessarily in the same patient. Both mani

in 2 instance just knicking the diseased bowel wall accidentally during operation resulted in immediate fi tula formation in the healing incision even though great surgical care was immediately exercised in suturing the cut in the wall of the ileum

Spontaneous fi tulas to the abdominal wall without a previous laparotomy have not been observed But unusual exit sites for external fistulas are occasionally noted Multiple external fistulas to the inguinal region have been noted twice at least 4 fistulas in one instance there being no previous operative scar Hurst has noted a fistulous tract origi nating in the ileum and pointing downward and infiltrating the extra peritoneal tissues in the right groin Brown and Donald reported 47 cases with fistula formation out of a total of 178 cases an incidence of 26 5 per cent This is a higher incidence of fistulation than that encoun tered in this present series or in most of the current literature They further state that fistula formation occurs invariably only after surgical procedures

Ileo psoas fistulas to the lumbar region have been seen 3 times twice by the author and once mentioned and reported by Snapper where

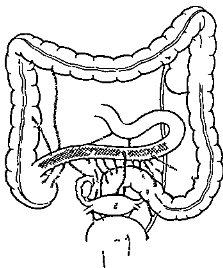


FIG 13 M ltiple fistula leum to adj ng hollow visce a N te termi nation in h al sites a right fallopian t b left ureter body of terus

Chapter 5 Fistula Formation In Regional Ileitis

FISTULA FORMATION is the most constant clinical and pathologic phenomenon in ileitis. These intestinal fistulas are of three types: (1) fistulas to the anterior abdominal wall; (2) internal fistulas between loops of bowel and adherent hollow viscera; (3) rectal and perirectal fistulas.

Fistulas to the anterior abdominal wall are among the most common types of fistulation and occur exclusively in the site of the scar of a previous laparotomy. The antecedent operation in most cases (30.6 per cent) was an appendectomy. We encountered 47 instances of anterior wall fistulas, all of them in the appendectomy scar or in the scar of a previous exploratory laparotomy. Fistulas to the abdominal wall are infrequent after simple appendectomy for acute appendicitis (Ginzburg). According to Colp, in 2840 cases of acute appendicitis abdominal wall fistulas were found only 33 times, an incidence of 1.1 per cent; only 3 required reoperation. Clark and Dixon in 44 cases of regional enteritis found 9 external fecal fistulas, one of which passed feces and gas through the urethra. Four of these 9 patients also had intraintestinal fistulas, one a fistula to the urinary bladder.

In some of the instances of ileitis not single but multiple fistulas were present; in one case 4 anterior wall fistulas in several scars of 8 previous laparotomies (Crohn).[7] These fistulas occur usually within a few weeks of the apparent healing of the operative scar. The scar becomes reddened and inflamed at a localized area, a low grade fever becomes apparent with regional pain and tenderness. An abscess forms and either breaks spontaneously or is incised, following which fecal drainage occurs and a chronic fecal fistula is established. In some instances the abdominal wall fistula occurs only months or years later, 2 years, 4 years and in one instance 8 years after a presumably successful resection for terminal ileitis. The 8 intervening years were marked by excellent health until the appearance of the fistula signalized a recurrence of the ileitis.

These external wall fistulas are apparently very facile of creation

segment of the large bowel or in any adjoining hollow intra abdominal viscus such as ureter urinary bladder uterus or fallopian tube

The internal fistulas were noted in 95 of our series (approximately 17 5 per cent) though the incidence of such internal fistulas would appear in practice to be much higher Variations of these internal fistulas are listed in table 7

TABLE 7

VARIATIONS OF INTERNAL FISTULAS

Site of fistula	*No of Cases*
Ileo-cecal	39
Ileo ileal	18
Ileo sigmoid	18
Ileo vaginal	4
Ileo psoas	
Ileo inguinal	1
Urinary (Ileum to urinary bladder)	1
Ileum to uterus	1
Total	95

On two occasions the opening of the fistula into the sigmoid colon was seen by sigmoidoscopy In two other instances the fistula which broke into the right fallopian tube gave rise to a salpingitis discovered inadvertently by a gynecologist operating for supposed adnexal inflammation The discharge of the proteolytic content of the fistulous tract into any hollow viscus usually terminates its course

Probably the most common of all these internal fistulas are those of the ileo-ileal variety they are readily demonstrated at the operating table (figs 14 15) Many or most of these fistulous tracts are notable and visible in the preoperative radiographic films provided that their presence is diligently searched for The fine lines seen with a magnifying lens emanating from the diseased ileum indicate potential fistulas (fig 15) These are frequently seen overlying the dome of the urinary bladder and creating urinary symptoms actual gross fistula exit into the urinary bladder is rare in ileitis much less common than are such similar fecal fistulas which arise in a sigmoid diverticulitis Forbes and Duncan report an interesting case of ileitis in which a large fistula existed between the terminal ileum and the urinary bladder the patient passed gas and fecal material through the urethra Ileo transverse colostomy without transection of the ileum was performed but the intestinal symptoms and those of the ileo vesical fistula persisted At a second operation

a series of external fistulas occupying the right lumbar area were observed expelling vegetable matter and fecal content. The fistulas were traced to a terminal ileitis. The linear extent of these intestinal fistulas gives rise to some speculation as to their nature. They are apparently lytic rather than infectious in type. They traverse large areas of mesentery and distal fascial planes without giving rise to infection, terminating their course by finding an exit point somewhere on the surface of the body. They are lytic or proteolytic, the activated intestinal or pancreatic enzymes of the fecal chyme slowly digesting their way through planes of fascia and muscle to exit on the body wall. Such fistulas become infected and suppurate only as a result of skin bacterial contamination at the point of exit from the abdominal cavity.

Internal Fistulas

The mechanism of formation of internal intestinal fistulas is identical to that of external abdominal wall fistula. These tracts originate in the sodden, porous, ulcerated terminal ileum, usually on the side of the mesenteric attachment. They traverse the mesentery of the small bowel and terminate in an adjacent loop of small intestine in any



Fig. 14. Combined ileocolitis. Note fistulous tract between ileum and base of cecum. Meckel diverticulum not involved.

Perirectal Fistulas

In 1934 Bissell published a case report of terminal ileitis in which multiple rectal fistulas occurred as a complication of the intestinal disease He felt that the presence of the inflammation of the ileum in the cul de-sac could easily have given rise to the rectal absces and persistent rectal fi tula In 1938 the diagnostic significance of perianal rectal and recto-vaginal fistulas was emphasized[2 0] (Penner and Crohn) In that publication 20 cases of perirectal fistulation were noted in a group of 110 cases of ileiti an incidence of 18.2 per cent Thi was almost equal to the combined number of external abdominal wall fistula (12 cases) and internal intestinal fi tulas (11 ca es) as shown in that serie The total incidence of fistula formation in this series of 542 cases can be summed up as follows

In the present series of 542 cases of regional ileitis perirectal abscesses and fistulas were noted 77 times an incidence of 14.2 per cent this does not include 9 instances of recto-vaginal fistulation The total number is somewhat below the combined number of external (47) and internal fistulas in this present series (95) which equals 26.2 per cent This equal 42 per cent of all cases[1]

TABLE 8

Type f Fi tula	*N of Ca s*
Exte nal abdom nal wall fistula	47
Ileo-psoa	2
U nary	12
Ingu nal	1
I ternal test nal to n ghbor ng v cera	79
Perirectal or e t vag nal	86
Total	227

Jackman and Smith in 1943 recorded 36 cases at the Mayo Clinic of anal abscess or fistula in a group of 114 cases (31 6 per cent) a figure high above those in this series They included those cases that had a history of operation for anal fi tula within a 3 year period prior to their initial visit Eight of the series of 114 cases came to the Clinic primarily becau e of anal fistula the intestinal disturbance being so mild as to have been overlooked



Fig 15 Terminal ileitis Fistula ileum to sigmoid

the ileum distal to the anastomosis was transected as the sole procedure except for a temporary ileostomy of the distal ileal loop Within four months the patient gained 25 pounds in weight and was free of symptoms while the dysuria and passage of gas and feces per urethra had disappeared Unfortunately a severe recurrence of the ileitis took place after the date of publication of their article In another case cited by these authors an ileo vesical fistula persisted for some time in spite of an ileo colostomy This fistulous tract was resected and broke down again with the secondary formation of an additional fecal fistula but eventually both fistulous tracts healed with subsidence of all symptoms

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TABLE 3

Type of Fistula	*No of Cases*
External abdominal wall fistulas	47
Ileo-psoas	2
Urinary	12
Inguinal	1
Internal (intestinal to neighboring viscera)	79
Perirectal (or recto-vaginal)	86
Total	227

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Fig 16 Peri anal fistulas in regional ileitis

Method of Anal Fistulation

Either of two method may explain anal suppuration

1 Most of the e fistulas occur as a result of infection in the rectal crypts of Morgagni above the anal sphincter the contaminated fecal infectious material being transported thereto by the propulsion of the fecal column The infection of the crypts gives rise to a perirectal abscess or an ischio rectal ab cess which opening simultaneously on the surface of the buttock and within the anal canal forms a permanent fistula When the abscess localizes anteriorly in the female it may break simultaneously through the perineal body into the vagina and po teriorly into the rectum forming a recto vaginal fistula

Thi type of local rectal infection in ileitis is almost identical to that seen in ulcerative coliti In both the internal opening of the fi tulous tract i ju t within the anal margin in the recto vaginal fistulas the anterior opening i ju t within and above the fourchette constituting a small opening which emit a thin fecal leakage

2 The second method of fistulation to and about the anus and perineum i more problematic Thi fistulas tract is considerably more circuitou *proteolytic material escapes from the porous terminal loop*

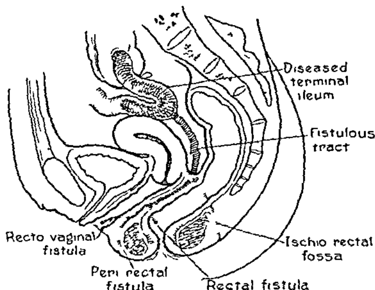


Fig 17 Gravity fistula—route of direct fistulation terminal ileum to perirectal space

of ileum lying heavily on the pelvic floor The material seeps downward through the pelvic peritoneal reflection and the retroperitoneal fat and burrows through the pelvic fascia following the planes of the levator ani muscle (fig 17) The material makes it exit into the rectum above the sphincters or piercing the slinglike attachments of the fibers of the levator ani makes its exit at the perianal margins The ischio-rectal fossa may be contaminated forming an abscess which will reveal itself as a perirectal fistula communicating internally with the rectum Attempts to follow such long fistulous tracts are difficult lipiodol injected into the tract from below will ascend for several inches but will be lost somewhere in the pelvis a streak of barium following a radiographic study may be seen pointing downward in the same direction A direct and continuous path has not been unequivocally *demonstrated except in one case in the literature* where at autopsy the continuity of the path was clearly dissected (Patricelli)

The diagnostic significance of perianal fistulas has not been sufficiently appreciated they may occur one to 14 years before the onset of active diarrhea and abdominal pain constituting the early prodromal manifestations of the disease

It is a fair statement to make as a generalization that suppurative perianal fistulas in the presence of diarrhea indicate a pathologic inflammatory process somewhere in the intestinal tract These fistulas occur with great frequency in ileitis ulcerative colitis and intestinal tuberculosis They do not occur in nervous gastrogenous pancreatic allergic or thyrogenic diarrhea Exceptions to this general rule have been very rarely noted

Chapter 6 The Course in Regional Ileitis

REGIONAL ILEITIS may begin as an acute phase of the disease or it may be first observed as an acute exacerbation of a pathologic process which has been overlooked In the vast majority of cases it comes under observation as a disease of great chronicity The acute case simulating acute appendicitis (except for the presence of diarrhea as a symptom) resolves in 66 per cent of the cases without further evidence of recrudescence The remainder of the acute cases subside spontaneously usually in spite of the laparotomy and customary appendectomy and lapse into the low grade typical chronic course of the disease

The course of long standing chronic regional ileitis is one of great chronicity Spontaneous remissions that endure for years may occur during which remissions the diarrhea will abate or be absent the temperature remain normal appetite be preserved and nutrition be only slightly impaired Except for a slight and slowly progressive loss of weight mild persistent anemia and occasional short bouts of diarrhea and abdominal pain the patient may follow a normal career of physical well being and school or occupational activity If the disease intensifies in the intestinal tract the period of activity will be greater and will last longer the remissions become shorter In time either the continuous diarrhea or the loss of weight and strength will indicate the progression into a most severe phase of the disease Eventually the onset of obstruction (45 cases(will supervene with abdominal pains vomiting and the ability to feel an abdominal mass on palpating the abdomen At any time in the course of the disease a perirectal abscess or a fistula in the scar of the abdominal wall may supervene

In the continued study of chronic regional ileitis with the assistance of radiographic observation it will be noted that three variations in the course must be considered In the first group spontaneous healing of the lesion with disappearance of all radiographic evidence will supervene This occurred in 5 of this series of 542 cases of regional ileitis The second group is constituted of cases in which anatomically the lesion remains static usually localized to the terminal ileum progression up-

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have however been observed radiographically to show the lesions remaining stationary. Thi applies even in cases where skip lesions are already demonstrable



FIG 18 Te m nal ileit con ervat ve m d cal th apy At onset— volve m nt of 12 inch s of ileum

C e D \ A 34 yea old w m n w th reg al l it Th olveme t of the le m was demon trated rad g aphicall n

January	24	1953	di t l 12 14 nch
Ju e	9	1953	12 14
No emb	15	1954	12 14

ward of the pathologic process cannot be radiographically demonstrated In the third group the lesion is obviously a progressive one and continues to spread mildly either continuously or by skip lesions until the upper reaches of the ileum or the jejunum become involved

Group 1 (5 cases)

Chronic Long standing Regional Ileitis with Spontaneous Healing

It was surprising to note that spontaneous healing with roentgeno graphic proof could take place in regional ileitis even in ca es where internal fistulation had been radiographically demonstrated In these 5 cases the diagnosis had been first observed and confirmed at the time of previous appendectomy For example

1 A woman 32 years of age with a fistula to the abdominal wall a tubo ovarian absce s and a palpable mass Radiographically 2 3 feet of ileum were involved She was well after 4 years
2 A man 45 years of age the whole ileum was involved He was well 3 years later
3 An 18 year old girl with involvement of the mid ileum and jejunum with clubbing of the fingers Three years later under meticorten therapy she was well and a radiographic study of the small bowel was negative
4 A 20 year old female with involvement of 10 inches of mid ileum She was well and the radiographic study wa negative 3 years later

It will thus be observed that in a minority of fortunate individual an apparent spontaneous cure is possible fistulas internal and external under exceptionally favorable conditions are capable of self healing Restoration to normal health and well being seems possible

These ob ervations on self healing are made with the reservation that relapses have been noted even after as long as 9 to 27 years of apparent health and in spite of apparent surgical cures The final word on the life history of the di ease as pertains to self healing may require future elaboration

Group 2

Chronic Regional Ileitis without Progression (fig 18 20)

The exact percentage of ca es in thi group cannot be stated since comparative radiographic studie over the cour e of years is not often capable of fulfillment (figs 21 and 22) A sufficient number of ca es

have however been ob erved radiographically to show the lesions remain ing stationary This applies even in cases where skip lesions are already demonstrable



FIG 18 T mi al l t conserv tive medi al ther py At onset—involvement of 12 inch s of il um

Ca e D K A 34 ye r old w ma with reg nal ileit The involvement of the le m wa dem n t ated rad g aphically on

Jan ary	24	1953	d tal 12 14	nch s
June	9	1953	12 14	
November	15	1954	12 14	

Case D R An 18 year old girl with the following radiographic studies

November 26 1948	Terminal ileum negative
September 25 1950	Questionable involvement of terminal ileum
December 8 1950	Terminal 6 inches involved
March 16 1951	
October 3 1956	" "

There was some evidence of healing the lesion was regarded as minimal in extent and depth

Case E H A 35 year old woman whose x ray studies were as follows

October 15 1955	Two loops of distal ileum involved
November 12 1955	
July 31 1956	
February 4 1957	



Fig 19 Seven months after onset

These are typical examples demonstrating the fact that the disease chronic and granulomatous in nature will remain without progression upward for long periods of time if not indefinitely

These cases without extension of the disease over the course of



Fig 20 One year and two months after medical treatment Note No progression of lesion anatomically

years seem to lend themselves best to surgical intervention While late intestinal obstruction is often characteristic of this chronic type recurrences after operation are less likely to occur This group should be the most satisfactory for surgical care In one case the lesion was recognized at exploratory operation 18 years ago the true nature was not recognized and no further surgical intervention was attempted The disease lay dormant and presumably asymptomatic Recurrence of diarrhea and a positive x ray picture led to operation and resection of the persistent and unextended lesion in the terminal ileum



FIG 21 J G Regional ileitis 1951

Group 3

Chronic Regional Ileitis with Progressive Extension (Mucosal Type)

These are the cases in which the study of the life history of the disease over a course of years reveals active progression of the lesion in an oral direction Again there are insufficient personal observations to allow any percentages to be offered but an occasional observed case is illuminating

Case 1 *M H* Male aged 42 In 1935 exploratory operation for terminal ileitis fistula in ano Eight to 10 inches then involved no resection In 1943 8 years later whole ileum involved up to jejunum Hypoproteinemia marked emaciation



Fi 2 J G Same case 1957

C e 2. (*figs* 3 26) *M H* F mal m ried 51 yea s of age F st seen June 1947 For the la t 13 months uffered with mild diarrhea and attacks of bloating and of abdom nal c amp he had been con tantly ncomfortable after eat g. Sh had tained a lo of 30 pounds in weight n the last 6 mo ths The date and th re lt of the va ious rad ograph c xam nat o w e a follow

Oct b r	1946	8 10 nch s of termin l ileum nvolved
Ma ch	1947	10 1
J ne	1947	18
Decemb r	1947	60 "

In this last case in which the succes ive radiographs were present for comparison the oral progress of the lesion was capable of clear demonstration (figs 23 26)

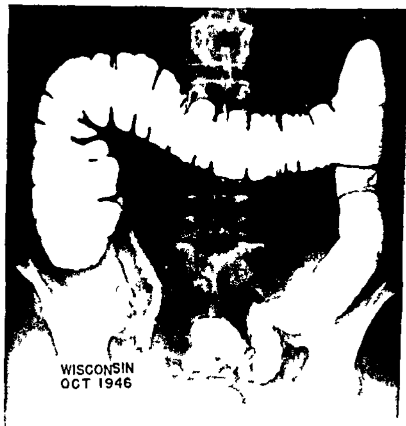


Fig 3 Octobe 1946—terminal ileum
Figs 23 26 Mucosal or submucosal type of progressive ileitis Observations extend for little more than a year

In this present series there are only 7 instances of rapid progression of the disease the so called mucosal type One case after a 7 year follow up was well 5 of the cases continued to be severely ill one case died All in all one gains the impression that the rapidly spreading mucosal type of the disease presents a poor prognosis

It is likely that it is the so called mucosal or submucosal type of case that gives the disappointing re ults after surgical therapy the rapid progression probably indicates that much more of the upper bowel is involved than is demonstrable on the x ray films

In the chronic case of regional ileitis remi sion of long periods may be ob erved such periods between recurrences of diarrhea and fever

Fig 24 April 1947—two terminal loops involved



Fig 25 June 1947—whole ileum involved



FIG 26 November 1947—whole ileum and lower jejunum

have been noted to cover up to 5 and 10 years In one case the onset of symptoms dated 8 years after a previous appendectomy due supposedly to chronic appendicitis In the later stages of the disease the symptoms become increasingly severe the recurrences more frequent and of longer duration until continuity of severe complaints causes complete disability

Chapter 7 Complications of Regional Ileitis

Perforation of Intestine

ACUTE FRANK PERFORATION with generalized peritonitis is extremely rare but can occur. Slow walled off perforation is manifest particularly in the acute instances, 8 cases in this series. In the chronic cases it is not uncommon for laparotomy to reveal a walled off abscess about the inner surface of the terminal ileum limited by the neighboring loops of ileum and the mesial wall of the cecum, the whole being agglomerated in one confused mass. When the loops of involved ileum are separated there may be a gush of a small quantity of pus. The neighboring loops are covered with a fibrinous shaggy peritoneal deposit; a small quantity of inflammatory cloudy fluid may be present in the peritoneal cavity (300-400 cc.). The granulomatous low grade type of infection with concomitant fibroblastic reaction precludes the occurrence of free open perforation with only rare exceptions. Attempts to resect terminal ileitis in the presence of a walled off abscess with localized peritonitis is fraught with a high operative mortality. Arnheim reports acute perforation of five days' standing in a chronic ileitis; death occurred before operative interference. Two perforations of the terminal ileum were observed with localized abscess and peritonitis.

Hemorrhages

Gross hemorrhage was noted in 25 instances in this series, usually in the course of the disease, occasionally (twice) as an initial symptom. The hemorrhage usually occurs in the form of a melaena (23 instances); twice hematemesis was noted, once as an initial manifestation of the disease. Fallis quotes a case with repeated profuse and massive hemorrhage passed by the bowel (melaena); two previous x ray examinations had been negative. Eight transfusions were required to control shock. Eventually at operation 27 inches of ileum were resected with cure. Galambos and Mittleman cite a case of atypical terminal ileitis in which gastric hemorrhage and melaena dominated the clinical picture and led to the presumptive diagnosis of a peptic ulcer. Yunich and Crohn reported

the case of a 55 year old male whose onset of symptoms was ushered in by two massive intestinal hemorrhages in the form of melaena producing syncope and collapse The second hemorrhage was almost fatal

Since one now accepts the fact that the duodenum and even the stomach can be involved in the inflammatory process we must also look to the upper gastrointestinal tract for a nonspecific cause for hemorrhage This problem is further complicated by the fact that duodenal ulcer occurred in 18 and ga tric ulcer in 2 of our cases While there is probably no relationship between the incidental finding of peptic ulcer and ileitis gross hemorrhage in the course of ileitis may be complicated by the presence of an existing or preexisting peptic ulcer of the usual variety

General Complications

Peptic ulcer was noted 20 times cholelithiasis 3 times and acute cholecystitis was encountered once during an operation for terminal ileitis Regional enteritis involving a Meckel s diverticulum has been observed (Horn and Rhoads) in one case with perforation at the ba e of the sac In our own series we have once seen Meckel s diverticulum involved in a skip lesion In another case a Meckel diverticulum causing low intestinal obstruction by torsion was clinically preoperatively mis taken for a case of ileitis Patricelli also mentions a case of regional ileitis with Meckel s diverticulitis with fatal outcome

Some general complications that occur are actually incidental and not related to the di ease Thus this series includes 4 cases with chronic rheumatic heart di ease one with a decompensated right heart on the ba is of generalized arteriosclero is In 17 cases in this series arthriti occurred as a complication the large joints usually being involved one ca e involved the cervical pine In 7 in tance erythema nodosum on the lower extremitie wa al o vi ible Von Patten observed polyarthriti of the rheumatoid type in 27 (4 5 per cent) of his series Infectiou mononucleosis occurred in 6 individuals as an intercurrent disea e In an unusual case active pulmonary tuberculosis was present though the re ected ileitis was characteri tically of the nonspecific granulomatous type in thi ca e too diffu e involvement of the large joints was noted Infantili m and delayed exual maturity has already been mentioned One ca e ob erved had had a large retroperitoneal or intra abdominal abscess with con equent ob truction of the inferior vena cava

Tetany in regional ileiti i uncommon occurring more frequently in tho e ca es of diffuse di ea e involving the upper ileum and jejunum

One case following two resections of the small bowel for recurrent ileitis developed typical carpo pedal spasm Blood calcium in this case was 6 7 milligrams per cent Immediate relief was noted upon injection of calcium gluconate and control of the diarrhea In another case typical tetanic convulsions were noted with a blood calcium of 3 4 milli grams per cent Renal calculus occurred 7 times in this series

Amyloidosis does not occur in any of the cases in this series in pite of the long duration and chronicity of the disease This is probably due to the nonpygenic nature of the discharge from the surface fistulas or in the intestinal flux

Primary amyloidosis of the alimentary tract ha been reported by Golden in a Negress observed for 16 years who e presenting symptoms were hematemesis dyspnea and orthopnea At autop y the stomach duodenum and terminal ileum were all involved the liver spleen kidney and adrenal were free of amyloid This however is different from true primary regional ileitis in which the systemic amyloidosis is a sequel or a complication In primary systemic amyloidosis the gastro intestinal tract may be involved as may any other organ involvement of the arterioles and of the stroma occurs frequently in the intestine How ever systematic amyloido is secondary to ileitis or nonspecific ulcerative colitis is extremely rare (Koletsky and Stricker Moschcowitz Cohen and Fishman)

Gaucher s disease was seen in a case of ileitis as an incidental find ing Pernicious anemia was een in one case in this series in a man 54 years of age who had undergone a short circuiting operation for regional ileitis followed promptly by a recurrence of diarrheal symptoms At a second operation the original site of the di ease the terminal ileum and the ascending colon were re ected but no recurrence of the disease process in the new proximal ileum was noted An unusually severe anemia and emaciation followed this operation Two years later the blood count revealed a true primary pernicious anemia hemoglobin 26 per cent RBC 1 400 000 WBC 2 650 cells myelocytes one normo blast marked anisocytosis and poikilocytosis hematocrit 10 8 per cent total proteins 4 6 per cent Sternal marrow puncture 38 per cent myelo blasts The administration of liver extract was followed by a dramatic response of reticulocytes to 30 per cent On discharge the hemoglobin was 60 per cent total proteins 6 1 grams per cent

According to Argentinian writers [9 3] osteomalacia is not uncom mon in all disease characterized by disturbance of fat absorption and

affects mostly the lumbar spine In 2 cases of regional ileitis the osteoporosis was present in a discreet form in the lumbar vertebrae

Despite the severe suppurative intra abdominal complications which accompany walled-off perforations in ileitis pylephlebitis and multiple liver abscesses are rarely seen The report of Snavely is the only one to be found in the literature a Negro male suffered with diarrhea and high fever ascites was probably present On one occasion only cysts of ameba histolytica had been found At examination regional ileitis involving 5 feet of ileum was noted a fistulous communication between terminal ileum and the sigmoid was present as also were pylephlebitis and multiple small liver ab cesses No such complication of ileitis is seen in this serie probably for the reason that almost all cases are instance of granulomatous rather than of suppurative disease Warren and Sommers quote an additional case in a Negress in which autopsy di closed thrombosis of the inferior vena cava and external iliac veins following upon intestinal obstruction and complicated by numerous internal fistulas They mention also one case of mucous cell carcinoma in regional ileitis In the present series we too have ob erved one case of adeno-carcinoma in a typical in tance of ileo jejunitis the carcinoma was situated in the mid jejunum Intu su ception is not mentioned in the literature as a complication of ileitis

Gynecologic Manifestations

There is little disturbance of endocrine function in the female as a result of ileitis Menstruation is not affected even in the severe cases This is in contrast to ulcerative colitis in which amenorrhea is a frequent manifestation of the severe and toxic phase of the disease the return of the men es usually indicate the improved prognosi and the beginning of a remi sion

Fertility is unaffected by ileiti pregnancy having been noted frequently in this erie particularly during the remission

Pregnan y as a C mplicatory Factor in Ileitis

It ha by now been fairly well e tabli hed that ulcerative colitis and pregnancy are poor conc mitant Patients with active colitis who become pregnant do badly Even inactive coliti ca es in the presence of ge tation may have a stormy cour e and if they pass the second and third trimester without a recurrence they frequently suffer during the

postpartum period Colitis arising de novo during the pregnancy or in the postpartum period are likely to be serious cases

What is the result when an ileitis patient becomes pregnant? Our experience as published in 1956 (Crohn Yarnis and Korelitz) comprises a study of 84 pregnancies in 53 patients who either had had ileitis or had ileitis at the time of fecundity These cases were divided into four groups for comparative purposes

Group I Known ileiti whose disease was *inactive* at the time of conception There were 34 patients who had 45 pregnancies during a quiescent period of the disease Twenty-eight or 62 per cent had uneventful pregnancies 7 had a recurrence of the disease during the carrying period 10 had po tpartum recurrences of active symptoms making 38 per cent unfavorable

Patients who had had prior surgery did better 81 5 per cent came to term without recurrence of the symptoms of the disease In this group patients without prior surgery fared poorly only 27 7 per cent survived the pregnancy without a recurrence of active symptoms Most of the recurrences took place in the econd and third trimesters (6) and an equal number in the early postpartum months The advantage of prior surgery is quite evident

Group II Ileitis *active* at inception of pregnancy This group comprised 23 patients with 30 pregnancies at a time when the ileitis was in an active phase In 3 instances the ileitis was mild in 22 it was moderately severe and in 5 it was markedly active at the time of conception

Of these 30 pregnancies in 14 the di ease subsided in 12 the course of the disease remained unchanged aggravation of the course of the pathologic process was observable in 4 in tances But of the 14 cases that passed through an uneventful course during gestation 10 of them had postpartum recurrences Those without prior surgery fared fairly well In 26 per cent of the 30 pregnancies in thi group the course of the pregnancy was unaffected by the intestinal disease but 12 of these successfully terminated pregnancies showed postpartum recurrences

Group III Ileitis *beginning* during pregnancy This group comprised only 3 cases In this group there were no full term pregnancie The only fatality in the entire series took place in this group Regional ileitis beginning during pregnancy constitutes a serious threat to both fetu and mother

Group II Ileitis beginning in the postpartum period This group comprised 6 cases the disease appearing usually immediately postpartum or in the first or second months following parturition Four of these patients soon improved one required surgical intervention and 2 have continued with mild recurrences of ileitis In general postpartum ileitis follows a relatively mild course

Broadly one may say that colitis constitutes a much greater threat to the health and occasionally to the life of the gravid mother While the question of therapeutic abortion is often raised in the colitis case that issue is rarely a factor of debate in the ileitis case In both ulcerative colitis and ileitis the proportion of abortions miscarriages and stillbirth does not exceed those in the control population

Chapter 8 Radiographic Diagnosis of Regional Ileitis, Ileo-Jejunitis and Ileocolitis

by Richard H Marshak M D *

SEVERAL INVESTIGATORS have divided the roentgen finding in this disease into acute subacute and chronic stages Since the classical form of regional enteritis is that of a low grade inflammatory process with episodes of acute exacerbation it is difficult to identify such a clear-cut pattern Acute granulomatous regional enteritis has been described but the determination of the precise time of onset of this disease is unusually difficult

Roentgen demonstration of proximal and distal extension of the disease process despite repeated examinations extending over a period of many years has not been observed The maximum length of involvement was determined on the initial roentgen studies This is not true after exclusion operations when recurrent disease is not uncommon

One of the prominent features of this disease is the development of stenosis with obstruction Therefore roentgenologically the cases may be divided arbitrarily into stenotic and nonstenotic groups It is difficult to classify these groups as early and late since the majority of cases may continue without stenosis for many years Again division into active and inactive seems inappropriate as the patient with long segments of stenotic bowel may also exhibit considerable evidence of clinical activity manifested by fever diarrhea and abdominal pain

Nonstenotic Phase The roentgen findings closely parallel the pathologic features The earliest mucosal alteration are blunting flattening and thickening of the valvulae conniventes The folds are arranged in a fairly regular symmetrical parallel fashion and as progression occurs may become thicker irregular and partially fused (fig 27) The bowel lumen becomes irregular in width These changes are due to the inflammatory submucosal and mucosal thickening When ulceration

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SEVERAL INVESTIGATORS have divided the roentgen findings in this disease into acute, subacute and chronic stages. Since the classical form of regional enteritis is that of a low grade inflammatory process with episodes of acute exacerbation, it is difficult to identify such a clear-cut pattern. Acute granulomatous regional enteritis has been described, but the determination of the precise time of onset of this disease is unusually difficult.

Roentgen demonstration of proximal and distal extension of the disease process, despite repeated examinations extending over a period of many years, has not been observed. The maximum length of involvement was determined on the initial roentgen studies. This is not true after exclusion operations when recurrent disease is not uncommon.

One of the prominent features of this disease is the development of stenosis with obstruction. Therefore, roentgenologically, the cases may be divided arbitrarily into stenotic and nonstenotic groups. It is difficult to classify these groups as early and late since the majority of cases may continue without stenosis for many years. Again, division into active and inactive seems inappropriate, as the patient with long segments of stenotic bowel may also exhibit considerable evidence of clinical activity, manifested by fever, diarrhea and abdominal pain.

Nonstenotic Phase. The roentgen findings closely parallel the pathologic feature. The earliest mucosal alterations are blunting, flattening and thickening of the valvulae conniventes. The folds are arranged in a fairly regular symmetrical parallel fashion and, as progression occurs, may become thicker, irregular and partially fused (fig. 27). The bowel lumen becomes irregular in width. These changes are due to the inflammatory submucosal and mucosal thickening. When ulceration

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FIG 7 The folds are thickened blunted and in some areas fused The contour is irregular There is rigidity and separation of the loops of intestine The intestinal loops appear straightened or uncoiled Diagnosis Nonstenotic type of regional enteritis

occurs a more characteristic pattern is produced Longitudinal streaks of barium recognizable as ulcerations appear (fig 28) As the thick blunted folds of mucosa are further destroyed cobblestoning may be noted (fig 29) This specific pattern is more common in the jejunum probably because of the thicker valvulae in this region Ulceration continues at the expense of the intervening islands of mucosa replacing the cobblestone pattern by an irregular network of interlacing streaks of barium The appearance at this stage has no uniformity or symmetry and is hazy and reticulated Denudation of the mucosa is usually incomplete leaving behind islands of inflamed mucosa which produce multiple smooth defects of varying size (fig 30) Their prominence is increased by the narrowing of the bowel lumen which is due to beginning cicatrical contraction that occurs at this stage Finally one may see the radiologic image of a uniform rigid castlike tube filled with barium and present



FIG 28 Longitudin l t ak f bar m i d cat g ulceration are een The cont r i r g la w th som g d ty and pa at n of the loops of sme t ne Diagn is Non ten ti type f eg onal ente ti

ing no mucous membrane pattern This i similar to ulcerative coliti and represents the stage when scarring and regeneration of an atrophic muco a is progres ing (fig 31) As scarring proceeds the transition to the stenotic pha e occurs An un ommon but striking finding is the presence of large inflammatory polyps (fig 32) Ordinarily the polyps are much smaller Carcinomatous transformation of these polyps ha not been observed Coincident with changes in the mucosa other charac teri tic roentgen features occur The bowel lumen reveals varying degrees of narrowing (fig 27) Early the submucosal thickening and as ociated spasm are responsible for the narrowing of the lumen Later as fibrosis occurs the narrowing i more marked and lead finally to the stenotic

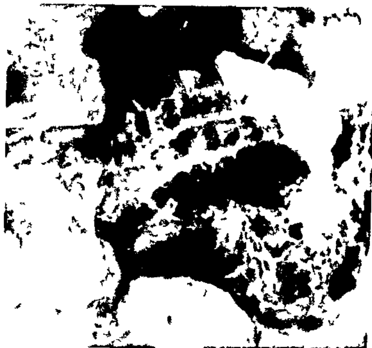


Fig 29 A cobblestone pattern is noted In other areas the folds are thickened and blunted The loops of intestine are moderately rigid and somewhat separated Diagnosis Non stenotic type of regional enteritis

stage (fig 34) In the early stages rigidity of the contour and mucosal pattern is incomplete Some flexibility or dynamic activity is evident in the change in contour and mucosal pattern during successive roentgenograms (fig 27) Later the roentgen appearance is fixed and unvarying (figs 31 34) *Pliability is lost Also early in this disease the normal* serpentine or coiled pattern of the loops of small bowel disappears The diseased segments appear to be straightened and rigid (figs 27 30) This finding is probably the result of loss of flexibility of the bowel wall and mesentery as well as longitudinal shortening due to spasm

Frequently the loops of intestine appear to surround a mass (fig 28) Although this may be due to an abscess resulting from perforation more often it is secondary to the indurated mesentery associated with the marked increase in the mesenteric fat and the enlarged lymph nodes Because the intestine is diffusely ulcerated and contains exudate and



Fi 30 Th e i rigid ty epa at on of the l ops of ntest ne nume o s mall fill ng defect d e to nflammato y polyps and cc ntr c sk p area Diag n si Nonstenotic f rm of ileo j j it

excessive secretions and the barium does not adhere to the walls the silhouette of the inte tine may be hazy De pite the increase in intestinal content the barium mixture remains fluid and homogeneous Agglutination clumping or formation of masses of barium is not found in regional enteritis as contrasted with the findings in the so-called prue pattern Segmentation such as is characteri tic of sprue has not been ob erved When unequivocal segmentation occurs the diagnosis of regional enteritis should be suspected Skip areas (fig 30) that is segments of normal intestine intervening between diseased segments represent another characteri tic feature The length of a skip area may vary from a few inches to several feet The extent of involvement on a



Fig 31 The loops are rig d and ma kedly separated The mucosal pattern appears ca tlike Several small filling defects are noted due to inflammatory polyps Diagnosis N n tenot c type of ileojejunitis

roentgenogram may be quite accurately determined in most cases since the transition of disease to the normal intestine is fairly abrupt An outpouching of the mucosa between the thickened fold (fig 33) occurs in some cases creating an appearance suggesting large diverticula This



FIG 32 Large fill ng def cts There a moderate degree f r g dity w th eas of na row ng The loop a epa ated D ag o No tenotic type of l j junit

i peculiar in that it seems to affect one side of the intestine and not the other These pseudodiverticula probably represent small eccentric skip areas

Stenotic Phase In the stenotic stage many of the rigid loops de scribed previou ly become constricted to a remarkable degree These stenotic segments resemble rigid pipestems (fig 35 37) This appear ance i due to a marked thickening and contraction of the wall of the mall inte tine The steno i may extend through 1 or 2 cm or over long segments With severe narrowing dilatation of the proximal in te tine may be marked In many instances it i difficult to state whether or not intrin ic di ea e is pre ent in a dilated area Very often di ease is present when a loop of dilated intestine exists between two points of



FIG 31 The loops a e igid and ma kedlv eparated The muco al pattern appears ca tlike Several small filling defect a e noted due to inflammatory polyps Diagnosis Nonstenotic type of ileojejun t

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FIG 34 Same patient a n figu e 3? ten years later At this time the lumen of the nte t n is narrow d The filling def cts previously described are not a prom nent Th re i no evidenc of an inflammatory mass Diagnos s Sten tic pha e of leo jej nit s

The loops are rigid and main ain a constant position from film to film Fistulas usually involving the distal ileum are frequent (fig 41) O casionally these are very difficult to demonstrate especially when dilated loops of intestine produce overlapping The fistulas may extend to and penetrate the abdominal wall

In general the roentgen findings in regional enteritis are as described however there are certain characteristics which are peculiar to the area of involvement

Ileum The mo t frequent site of involvement of the small bowel with regional enteriti is the terminal ileum (figs 39 40)

The trin ign which ha come to be identified a the pathog



FIG 33 The diseased loops of intestine are moderately rigid and separated The folds are thickened and blunted Pseudodiverticula are present Diagnosis Nonstenotic type of regional enteritis

constriction On the other hand when there is a single area of constriction with proximal dilation disease may not be present in the dilated segment However because of retained secretions secondary inflammatory changes tension ulcers and muscular hypertrophy the appearance of the dilated loops may be confused with the alterations seen in regional enteritis This distinction is of great importance when considering surgical therapy Some cases have not undergone operative intervention because the surgeon was of the opinion that the entire intestine was involved Extreme dilatation of the intestine for long segments is rarely associated with intrinsic granulomatous disease

Many of the roentgenographic phenomena observed in the nonstenotic phase of the disease are again noted in the stenotic phase The mucosal pattern is usually reticulated or castlike Small filling defects inflammatory polyps irregularly distributed throughout the diseased segments are noted Skip-areas and wide spacing between the segments of intestine are more striking (figs 35 38)

nition of the fact that the string sign does not always indicate marked fibrosis and stenosis is important since exclusion operations during the stage of marked ulceration and activity have been followed by a high degree of recurrence

Because of the marked ulceration fistulas and perforation (fig 41) thickening of the mesentery and separation of the loops of bowel are more frequent in the distal ileum than in the remainder of the small



Fig 36 The distal jejunum and proximal two thirds of ileum showing long areas of narrowing alternating with areas of dilatation The mucosal pattern in the stenotic areas is reticulated The loops of intestine are widely separated a d g d D gn St n ti pha of il o jej ti

bowel A possible explanation of the marked ulceration in the distal ileum may be the higher bacterial content in this area Deformity of the cecum and ascending colon is not unusual with involvement of the terminal ileum The deformity is most often due to the intense inflammatory process in the mesentery and to fistulas arising from the terminal



FIG 35 The mucosa is castlike with inflammatory polyps The affected loop is rigid and narrowed with an associated inflammatory mas Diagnosis Early stenotic stage of ileo jejunitis

nomonic roentgen manifestation of regional enteritis i most frequently noted in this area It has been described as a thin linear shadow suggesting a frayed cotton string in appearance (fig 39) The cau e of the string sign is incomplete filling due to irritability and spasm associated with marked ulceration and may be seen in both the nonstenotic and stenotic phase of this disease Repeated spot films will demonstrate the fact that some distensibility is still present in this segment (fig 40) The bowel proximal to the string sign may or may not be dilated depending on the stage of the di ea e In the nonstenotic phase the proximal intestinal lumen is generally not dilated despite the marked narrowing as ociated with the string sign indicating the importance of spasm in producing this characteristic appearance This spasm i usually inconstant When persistent temporary proximal dilation can occur with symptoms of obstruction In the stenotic phase there is constant proximal dilatation which may be accentuated by spasm secondary to ulceration Despite the narrowing complete intestinal ob truction i rare The recog



Fig 38 Long rig d nar ow d segm nts resembl ng pipe tems w th a large inflammatory mas D agno i Sten tic pha e f reg onal enteritis

vention until recently has been rare and long follow up of the natural course of the disease has been possible The transition from the non stenotic to the stenotic stage could be observed in the average case the interval was approximately four to five year In the stenoti phase the proximal bowel may become hugely dilated In these cases unless adequate amounts of barium are administered the exact ulcerations may not be identified Partial intestinal obstruction in this group of patients is common however complete intestinal obstruction has not been observed

It i of interest that many of these patients with extensive involve ment of the intestinal tract despite numer us episod s of partial intestinal obstruction can maintain an adequate nutritional status (fig 43)

Jejunum Twelve cases isolated to the jejunum were studied In *every patient there was marked stenosis* Three types of stenosis have been recognized a single area of stenosis with proximal dilatation a



FIG 37 The entire small intestine is involved with alternating areas of constriction and dilatation There is separation of loops of intestine The mucosal pattern in some areas is castlike and in others reticulated The intestinal loops appear to surround ma se Diagnosis Stenotic phase of regional enteritis

ileum and extending into the right side of the colon (fig 42) In most of the cases the granulomatous inflammatory process ends abruptly at the ileocecal valve

Regional enteritis involving the terminal ileum does not always produce marked ulceration There are many instances in which the inflammatory process is minimal In these patients the roentgen findings reveal slight rigidity slight lack of distensibility and slight serration of the contour of the bowel

Ileo jejunitis The di tal half of jejunum and proximal half of ileum *are characteristically involved (figs 29 31 32 34) Skip areas* are frequent Large inflammatory polyp may be noted (fig 32) Ulcera tion is not as marked as in the terminal ileum and fistula formation is less frequent Because of the extent of involvement operative inter



Fig 40 Same pat nt a in fig e 32 a few minutes later ll trat ng di ten bil ty N t also pasm f c c n

in the remainder of the mall bowel Sidetracking operations have been uccessful in every case but one again pointing to the fact that recur rences are more frequent when the operation i performed in the presence of marked ulceration and fistula formation Isolated jejunitis in the



Fig 39 String sign in regional enteritis

second form with two areas of narrowing and marked dilatation of the bowel between simulating a closed loop obstruction (fig 44) and a third type with multiple stenotic segments and intervening dilatation of the intestinal loop (figs 45 46) The length of stenosis has been short varying from one to three inches Ulceration is minimal Fistula formation is uncommon and the thickening of the mesentery is not as marked as



FIG 40 Same pat nt a in fig re 32 a few minutes late ll strat ng di ten bility Note also pa m of cecum

in the remainder of the small bowel Sidetracking operation have been successful in every case but one again pointing to the fact that recurrences are more frequent when the operation is performed in the presence of marked ulceration and fistula formation Isolated jejunitis in the

nonstenotic stage has not been observed These patients apparently have minimal symptoms for many years and are not investigated until partial obstruction supervenes

Duodenum Four cases were studied The findings in the duodenum are essentially similar to those in the jejunum (fig 47) Moderate stenosis is present and the ulcerated areas are seldom deep or marked Two of these patients have an associated terminal ileitis (fig 48)

Recurrent Ileitis In general the recurrent lesion acts similarly to the original process The earliest roentgen findings are again thickening



FIG 41 Terminal ileitis with numerous sinuses and fistulas Some of these extended into the urinary bladder

and blunting of the fold progressing through the many stages through the stenotic phase *Fistula formation appears to be less frequent* The length of the lesion has no effect on the recurrence rate The colon is rarely invaded and the usual site is the new terminal ileum (figs 49 50) Recurrences also appear to be more frequent in tho e patients in whom the initial lesion reveals marked ulceration with fistula formation Many patients with early recurrent lesions may be completely asymptomatic

Healing in Regional Enteritis While spontaneous remissions and clinical improvement following a variety of operative and con ervative



Fig 42 Terminal ileitis with large fistula between terminal ileum and ascending colon

therapies is frequently observed there is not a great deal of information demonstrating radiologic and pathologic healing Patients who undergo reexploration following ileocolostomy can show a remarkable degree of healing of the involved segments of bowel and mesentery The ulcerations may disappear and the fistulae close Demonstration of improvement without operation is rare in this series Three cases however have been observed where remarkable roentgen changes indicating healing occurred (figs 51 52) Despite these instances of improvement the large majority of cases demonstrates the disease to be continuous (figs 32 34) Many years however may elapse before stenosis supervenes It should be pointed out that secondary changes may occur in patients who are clinically improved notably stenosing lesions and permanent loss of the normal small intestinal structure These changes are due to healing with scar formation

Regional Enteritis with Involvement of the Colon In most cases of regional enteritis the roentgen alterations appear to end abruptly at



Fig 43 Entire ileum involved with regional enteritis Lesion unchanged during 8 year observation

the ileo cecal valve In a few patients involvement to the hepatic flexure was noted (fig 53) In four instances skip lesions from ileum to transverse colon were seen and in one patient there was involvement as far as the sigmoid The roentgen alterations in the colon were remarkably similar to the lesion in the ileum and usually revealed marked narrowing of the bowel lumen In the patient where the disease extended as far as the sigmoid it was impossible to differentiate the colonic alteration from ulcerative colitis

Combined Disease Regional enteritis may be associated with ulcerative or segmental colitis The characteristic findings of regional enteritis are unaffected by the inflammatory disease in the colon whether ulcerative or granulomatous and present the alterations described previously consisting of narrowing of the intestinal lumen rigidity ulcer



FIG 44 The mid jejunum is involved with alternating areas of constriction and dilatation One loop of jejunum is greatly dilated Diagnosis Stenosing jejunitis

ation of the mucosa inflammatory polyps skip areas fistula and separation of the involved intestinal loops

In the majority of cases the inflammatory process is confined to the distal part of the ileum In some cases diffuse jejunoileitis was present It is important to differentiate regional ileitis from so-called backwash ileitis which may be associated with ulcerative colitis In backwash ileitis the narrowing of the intestinal lumen is not as marked as when there is granulomatous involvement The mucosa usually presents minimal ulceration fistula formation is rare skip areas are uncommon and marked separation of the intestinal loops is not usually observed (fig 54) In some cases of backwash ileitis however the ulceration of the mucosa



FIG 43 Entire ileum involved with regional enteritis Lesion unchanged during 8 year observation

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FIG 46 Greatly d lated segment f j jun m p o mal t an area of narr w ing in d stal jej n m D ag o Steno i g jejunit



FIG 45 Constricted segments starting at ligament of Treitz alternat ng with areas of dilatat on in jej num There is considerable dilatation of the duodenum The muco al pattern in constricted areas appears castl ke Diagnosis Stenosing jejuniti

is marked producing sufficient spa m as to result in the formation of the string sign This finding however is unusual and the degree of narrow ing and rigidity u ually seen with regional enteritis as ociated with proximal dilatation is absent

When the lesion in the colon is diffuse the roentgen alterations are similar to tho e u ually identified with diffuse nonspecific ulcerative colitis In the case where there i an a ociated segmental or granu lomatou coliti the finding are usually limited to the right side of the colon skip areas are not infrequent inflammatory polyps are larger and there is more marked narrowing of the bowel lumen



FIG 46 Greatly dilated segment of *jejunum p ox mal to an area of narrow* ng in d tal j junum D agno s Steno ng jejun t



Fig 47 Regional enteritis involving the second portion of the duodenum The terminal ileum was also involved



Fig 48 Regional nteriti involving the stomach The te m nal ileum was also in olv d



FIG 51 Terminal ileitis



FIG. 5 Sam pati nt one year later Note marked improvement in the appea ance of the term nal ileum The finding at th s tim are minimal



Fig 53 Regional enteritis with extension into the colon to the hepatic flexure

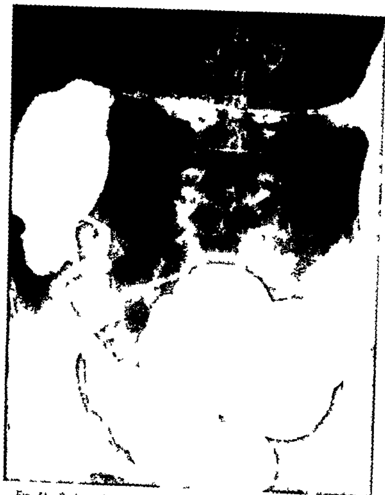


Fig 54 Right sided ulcerative colitis with involvement of the ileum (back wash ileitis ?)



FIG 53 Regional enteritis with extension into the colon to the hepatic flexure



Fig 56 Statu p tcol ctomy fo ulc rative l t w th ileo tomy Inflam matory d ease involving d stal ileum (nong anul matous)



FIG 55 Status postileosigmoidostomy with recurrent disease in rectum sigmoid and adjacent ileum

or more of these signs and symptoms should suggest the consideration of ileitis Diarrhea alone diarrhea plus fever diarrhea with fistula an abdominal mass with fever an intestinal or perirectal fistula or any combination of such symptoms and physical findings is suggestive An illustrative case in point is worth quoting because of it significance

> *P B* (Serial No 197) Male age 39 years For many years he had suffered with mild diarrhea Eight years ago he had been operated on for a rectal fistula Subsequently he had lost 59 pound complained of abdominal cramps and persistent diarrheal movements The physical examination was negative except for slight tenderness over the cecal area of the abdomen and suggestive clubbing of the fingers The rectal and sigmoidoscopic examinations were negative The radiographic examinations barium enema and barium meal were reported as negative except for some evidence of a spastic colon The terminal ileum was well visualized appears somewhat irritable in its distal portion but fills well and is distensible The report to the referring physician stated that although the diarrhea fever and the past rectal fistula strongly suggested ileitis the absence of confirmatory radiographic evidence made such a positive diagnosis impossible It was urged that the patient be carefully observed for future developments Six months later the patient developed a fistula from the ileum to the sigmoid At operation a regional ileitis was discovered involving 5 feet of ileum proximal to the ileocecal valve An ileo-transverse colostomy with transection of the ileum resulted in cure

The significance of the perianal fistulas cannot be overlooked In former years such fistulas either were regularly regarded as being tuberculous in nature or were suspected of a tuberculous origin Mummery in 1923 considered at least 15 20 per cent of perirectal fistulas to be of tuberculous pathogenicity In a survey of anal fistulas summarizing 600 cases Jackman and Buie found 87 8 per cent negative for tuberculosis In the true tuberculous fistulas primary affects elsewhere in the body usually the lung were always demonstrable This reversal in the viewpoint of the relationship of tuberculosis to anal fistulas is due in large part to the increasing role which ileitis and colitis play as etiologic factors in the incidence of such perirectal complications

It is particularly important to have sufficient mental fortitude to

Chapter 9 The Diagnosis of Regional Ileitis

THE DIAGNOSIS of regional ileitis is essentially a clinical one based upon the characteristic subjective symptoms and the physical findings The x ray diagnosis is valuable as confirmatory evidence and allows for anatomic interpretation of the lesion It is a grave error to think of ileitis as an obscure disease difficult or impossible to diagnose Ileitis has clear cut subjective and physical features which when combined spell out a succinct clinical diagnosis The combination of diarrhea fever anemia and fistulas internal or external with or without an abdominal mass with or without radiographic confirmation means a possible or a probable diagnosis of ileitis The negative sigmoidoscopy rules out the usual case of ulcerative colitis 95 per cent of which cases give a distinct pathologic sigmoidoscopic picture The remaining possibility is a right sided segmental colitis to be differentiated from regional ileitis Segmental colitis may and does have anal complications and rectal fistula but no fistulas to the abdominal wall and no internal fistulas or intra abdominal masses To recapitulate the diagnostic significance of the symptoms and signs of ileitis

1 The diarrhea is the most common feature being present in 95 5 per cent of the cases

2 Fever is frequent and significant but the majority of the long *standing low grade cases are afebrile*

3 Anemia may be so moderate as to be insignificant a hemoglobin reading below 65 70 per cent is of value

4 Loss of weight is significant but may not be extensive An abdominal mass may be present but most frequently is absent

5 Fistulas internal external and perirectal are the most nearly pathognomonic manifestation of the disease particularly when associated with diarrhea and with the other positive signs and findings of ileitis

The radiographic study is exceedingly important when positive a negative finding does not necessarily nullify a clinical tentative diagnosis of ileitis Any one symptom especially any combination of two

4 years during which time because of a soft systolic mitral murmur over the precordium the case had been con idered a one of chronic heart disease or subacute bacterial endocarditis in spite of repeated negative blood cultures Sprague et al report a case of long tanding fever in a girl of 15 year of age who presented the clinical picture of an irregular fever with temperatures ranging between 101 and 104 F with poly articular rheumatic like arthritic manifestation and perirectal ab ce e the whole clinical picture being due to a regional ileo coliti

The significance of the cardiac murmur may be overempha ized At least 5 case in thi serie had had rheumatic fever and bore re idual systolic mitral or aortic murmurs Add to the old rheumatic cardiac murmur a low grade fever and the po sibility of ileiti or segmental colitis i rarely con idered Thi i all the more important becau e in one ca e in thi series an acute endocarditis actually occurred as a com plication while the patient was under ob ervation A young woman with recognized regional ileitis wa under observation preparatory to opera tion An increa ed degree of fever wa a ociated with the development of a systolic murmur at the cardiac apex the murmur wa heard with daily increasing intensity a low rough murmur was audible and was transmitted to the mitral area A blood culture was negative at the height of the fever Penicillin was instituted the fever sub ided in 7 days and the cardiac murmur ceased to be audible The patient was later succes fully operated on for regional ileiti No further cardiac manife ta tions occurred

The larger and sometimes maller joint of the hands or feet may be implicated in diarrheal diseases the so called arthritis dysen terique but the significance of the arthritis a an intestinal manifestation is usually overlooked in favor of a diagnosi of rheumatic fever with joint involvement

The mild or moderate eosinophilia that frequently accompanies ileitis and colitis may sugge t and be confused with periarteritis nodosa

The eye complications which occur occasionally in ileitis but more commonly in ulcerative colitis again are u ually overlooked and are classified in the tuberculous or rheumatic category (Sprague et al) Ophthalmologi t of wide experience are con ciou of the fact that inflam matory lesion of the eyes are not uncommon complication of inte tinal disease Iriti iridocycliti keratitis corneal ulceration and phlyctenular conjunctivitis all constitute focal manifestations of intestinal diseases

sustain the diagnosis of at least probable ileitis even though many significant clinical features are missing and the x ray diagnosis is negative On several occasions one has been saved from a blatant error by including in the provisional negative diagnosis at least the possibility of ileitis The following experience is illustrative

The case was reported as nervous diarrhea irritable colon but the proviso was added of a possible ileitis Five years later the symptoms flared up and now exploratory laparotomy showed regional ileitis with an ileo sigmoid fistula Not that every case of diarrhea should be classed as a possible ileitis but the association of diarrhea with a fistula a mass fever or anemia or any such combination calls for diagnostic caution and acuity

The low grade fever of regional ileitis is often overlooked by general internists who are likely to pay little attention to mild diarrhea or to the complaints of occasional faint abdominal pain The patient may not consider two or three loose bowel movements as diarrhea the abdominal pain may be minimal and no positive physical signs may be discoverable These cases of ileitis with low grade fever are usually confused with brucellosis or undulant fever particularly when a low titer agglutination against the Melitensis organism has been reported Many a case of ileitis has been overlooked because of a positive agglutination of 1 40 or 1 80 against brucella One such case was even published in medical literature in this country (Sproull) as a case of undulant fever with unusual intestinal change this before the first description of ileitis as a clinical entity Years later exploratory operation and resection of the ileum revealed the true nature of the disease as one of ileitis with low grade fever the doubtful low grade agglutination titer against brucella having only confused the diagnostic issue

Ileitis which presents itself as a case of continuous low grade fever with low leukocyte count occasional joint involvement clubbing of fingers or eye complication especially when a heart murmur is present is likely to be overlooked this is particularly true when the minimal diarrhea which is the actual key to the diagnosis is ignored All of these manifestations of a generalized disease are common to both ulcerative colitis and ileitis omit the diarrhea and the general symptoms resemble brucellosis rheumatic fever subacute bacterial endocarditis lupus erythematosis disseminatu or Libman Sachs disease Rosenblatt Goldsmith and Strauss cite a case of regional ileitis unrecognized for



Fig 58 Hodgkin's Disease simulating ileitis

Intra abdominal Hodgkin's disease by its fever and low leukocyte count and its possible intestinal involvement may simulate ileitis Multicentric intestinal lymphosarcoma with its characteristic areas of intestinal dilatation its hemorrhage fever perforation and rapid wasting may be confused with ileitis Both Hodgkin's disease and intestinal sarcomatosis are intensely malignant and progressive diseases with early fatal issue in contrast to the more mild and low grade continuous course of chronic regional ileitis (figs 57 58)

The string sign of the terminal ileum may be simulated by hyper

Differential Diagnosis

When a suggestive string sign is present or when a disarrangement of the pattern of the intestinal mucosa is noticeable in the roentgenograms various other possible intra abdominal diseases come into consideration in the differential diagnosis When the upper ileum and the jejunum show puddling and segmental delays as well as disturbed mucosal patterns sprue and the vitamin deficiency diseases deserve close notice Here the differentiation between sprue and ileo jejunitis is often difficult (fig 71)



Fig 57 Lymphosarcoma simulating ileitis

the liver McLeod adds 2 cases to 283 reports in the literature (1944) intestinal obstruction in the terminal ileum and organ metastases were commonly ob erved Dockerty and Ashburn in a review of the literature describe carcinoid tumors (so-called) of the ileum They detail 30 cases of carcinoid of the terminal ileum 18 of which had metastasized locally or di tally small orange submuco al nodules were arranged linearly with a minimal degree of ulceration Regional lymph nodes were involved in 11 cases in 5 metastases to the liver were pre ent suggesting a low grade type of carcinoma virulence

Endometrial transplants on the sero a of the terminal ileum with or without inva ion of the intestinal walls occasionally may be confused with ileiti the string sign is almost identical The inte tinal bleeding with the men es may if pre ent suggest the true nature of the lesion A case of endometrio i a a cause of inte tinal obstruction has been described (McGuff et al) in which the segment 5 cm proximal to the ileo cecal valve wa involved by endometrial transplant The clinical picture resembled in general a ca e of regional ileiti with inte tinal obstruction

Enterogenous cysts about the ileo-cecal angle are exceedingly rare but may simulate roentgenographically the constriction of terminal ileiti (Rosenberg)

Actinomycosis intestinal with abdominal wall fi tulas may simulate ileiti the finding of the characteri tic ray fungu in the dis charges from the fistula will save much confusion and often embarra ment The possible confu ion between ileitis and arcoido i has already been discu ed (page 13) Sarcoido i of Boeck involving the small intestine as a granulomatous lesion was described by Watson and hi associates the identity of ileitis and sarcoidosis was even suggested by Hadfield Snapper however has made the point that he never encoun tered a case of sarcoido is with a le ion of the intestine nor have his many case of ileiti ever shown sarcoidosis Blackburn states that in ileitis there i no record of swelling of the fingers and toes lymph adenopathy or the uveoparotid syndrome such as is observed in typical sarcoido is Sarcoidosis is a generalized di ease affecting the reticulo-endothelial structural system Intestinal involvement by sarcoidosis with out generalized implication of other organs would be difficult to accept

Impairment of the blood upply to the intestinal tract may reproduce a clinical picture simulating acute or chronic regional ileitis the radio graphic picture of such a vascular lesion may be very confu ing Such

plastic ileo cecal tuberculosis carcinoid of the terminal ileum endo metriosis of the terminal ileum enterogenous cysts about the terminal ileum and actinomycosis intestinal

Primary intestinal tuberculosi as a manifestation of bovine infec tion is exceedingly rare in a complete survey of all the postmortem and surgical pathologic material at the Mount Sinai Hospital over a period of 15 years only 4 cases of primary intestinal tuberculosis were found to have survived a critical analysis (Crohn and Yarnis) In 2 of the e cases the ileum was the site of typical miliary tuberculosis tubercle bacilli were found in the sections of the histologic studies All other cases were those of ileo cecal or ileal tuberculosis secondary to open lesions in the pulmonary areas with caseating cavity formation and positive sputum or positive gastric residue findings for tubercle bacilli

Cases of regional ileitis regularly have negative chest finding by physical examination and by radiographic study Cases of secondary intestinal tuberculosis have strongly positive chest plates with evidence of cavity formation and with positive sputum findings That intestinal tuberculosis can simulate exactly the string sign of ileitis has been amply demonstrated (Crohn and Yarnis) This point has also been emphasized by Connell Blackburn found the Mantoux test negative in 19 of the 22 ca e and x rays of the chest uniformly negative in regional ileitis

Argentaphillic carcinoid tumors infiltrating along the muco a of the terminal ileum represent a favorite site for that le ion and can simulate the clinical picture and the radiographic string sign of ileitis In one case in my experience the terminal ileum was resected under the supposition that it represented a case of ileitis the gross specimen was passed from hand to hand and wa accepted as one of ileitis by many long-experienced in handling uch surgically resected specimens Only on histologic study wa the true character of the lesion identified as one of carcinoid tumor of the terminal ileum with metastase to the mesen teric lymph nodes

Up to 1939 237 ca e of argentaffine tumors of the small intestine had been reported in the literature obstruction occurred in 24 4 per cent of these Pennington and Priestly report a ca e of carcinoid tumors of the terminal portion of the ileum invading the me entery The abdomi nal ma s involved *several loops of the terminal segments of the* ileum The lesion was malignant everal meta tatic tumors being pre ent in

the liver McLeod adds 2 ca es to 283 reports in the literature (1944) intestinal obstruction in the terminal ileum and organ metastases were commonly ob erved Dockerty and Ashburn in a review of the literature describe carcinoid tumors (so called) of the ileum They detail 30 cases of carcinoid of the terminal ileum 18 of which had metastasized locally or distally small orange submucosal nodules were arranged linearly with a minimal degree of ulceration Regional lymph nodes were involved in 11 cases in 5 metastases to the liver were present suggesting a low grade type of carcinoma virulence

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Impairment of the blood supply to the intestinal tract may reproduce a clinical picture simulating acute or chronic regional ileiti the radio graphic picture of such a vascular lesion may be very confusing Such

circulatory disturbances may be secondary to a strangulated hernia or to volvulus or it may result from arterial occlusion venous thrombi or infarctions If such a pathologic process is limited to one segment of the small intestine and if spontaneous healing does ensue the radiographic representation may be one of isolated string sign or may indicate a segmental area of stenosis simulating true regional ileitis (Wolf and Marshak)

Chapter 10 Prognosis in Regional Ileitis Under Medical or Conservative Treatment

IN THE 1949 EDITION of this monograph only 13 out of a total of 222 cases of chronic regional ileitis were observed to undergo spontaneous healing or cure At that time some question was necessarily raised as to what constituted cure and what the durability was of such a so called cure or self healing This was a logical source for skepticism since the follow up of surgically treated cases showed late recurrences to take place as long as 9 14 or 17 years after what seemed to be a successful operation If the late surgical recurrences created legitimate doubt as to durability of cure how much more so would a follow up of medically treated cases raise the same scientific question of durability of long term beneficial results?

What constitutes so-called cure in regional ileitis? Not the roentgenographic picture alone for clinical improvement and disappearance of symptoms may be thoroughly achieved while the radiologic evidence may persist in showing string sign deformity and irregularity of loops of small bowel Can a true chronic granulomatous lesion of the intestine ever heal without lasting deformity in the roentgen films any more than a true penetrating duodenal ulcer with crater formation can ever return to the picture of a normal duodenal bulb as radiographically demonstrable?

The return of general well being, the restoration of weight loss the cessation of anemia and the reduction or disappearance of diarrhea constitute marked improvement in the subjective symptoms Add to this an inability to palpate a previously demonstrated mass and surprisingly even the healing of perirectal fistulas and one may be pardoned for regarding such a case as an instance of cure provided that the factor of time in the follow up is always borne in mind By cure if that term can be employed in such long standing disease is meant clinical betterment cessation of subjective symptoms and objective findings—not necessarily a return to a normal roentgenographic picture of the small bowel

By improvement one surmises a marked alleviation of symptoms a return to good nutrition diminution of diarrhea and ability to follow one s daily tasks and participate in family and public social activities

In this series of 542 cases of regional ileitis there were 111 cases roughly 20 per cent that were observed and followed under conservative observation over a course of years The conclusions in this series were unfortunately incomplete since 26 of the patients were lo t to follow up The results to date of the remaining 85 cases may be tabulated as follows

TABLE 9
MEDICAL FOLLOW UP (85 CASES)

Years	*Well*	*Improved*	*Unimproved*	*Died*
1	8	6	7	2
2	8	2	4	0
3	12	1	3	0
4	7	2	0	0
5	3	3	0	0
6 10	9	1	2	0
11 15	2	0	1	0
16 25	2	0	0	0
Total	*51*	*15*	*17*	*2*

At first one is surprised at the apparent large number of so called instances of cure 51 out of 542 cases or roughly 9 4 per cent in the earlier series of 1949 there were only roughly 5 per cent of spon taneous cure This improvement in figures may be due to two factor one a reluctance to operate as freely and as early in the course of the disease as in the previous years of surgical enthusiasm the other a possible improvement in medical care more diligence and patience in instituting conservative therapy and possibly or probably the extensive use of steroid therapy over longer periods of trial Note also that 15 cases were regarded as improved and 17 as unimproved and yet surgery was withheld in an attempt to protract the period of conservative therapy and thus avoid more drastic operative steps

In the last decade we have been passing through a period of warrant able skepticism regarding end results of surgical intervention the e larger numbers under conservative management reflect the current doubts as to the long range curative effects of operative interference And yet 51 cases observed over a follow up of from 1 to 25 years appeared to cured or free of symptoms and returned to health and well being

The true proportion is restored however when it is noted that the remaining 431 cases of this larger series had been subjected to surgical intervention and that these cases all represent the failures of conservative management. Nevertheless all in all roughly 10 per cent (actually 9.4 per cent) of ileitis cases do respond to medical therapy; this figure, small as it is, does constitute a plea for patience in the treatment of such cases and does seem to substantiate the opinion of those who are reluctant to submit to operation every case of ileitis as soon as the diagnosis is established.

In an occasional instance (5 cases) in this series "cure" was confirmed by the disappearance of roentgen evidence of the disease. These cases are however very rare and exceptional.

The duration of the "cure" as noted in the follow up is also of interest: while the majority of favorable cases have been observed for only 1 to 5 years there were 9 cases of "cure" that had lasted 6 to 10 years and 4 cases followed for 10 to 25 years that had remained well. This was an interesting and admittedly a surprising observation. Good as it is, it is only suggestive (but nonetheless encouraging) to those who advocate conservative therapy but it does not justify Bargen[14] who in a recent paper emphasizes an allergic etiologic factor in the disease and states that he and his colleagues have become "very conservative" in the surgical treatment of regional enteritis.

In the prolonged observation of cases of regional ileitis extended over the course of years deaths are not unusual. In our series of 542 cases there were in all 28 fatalities. Twelve of these were immediately operative or post operative; the remaining 16 cases died while under prolonged medical observation, just half of these due to the ileitis per se, the other half (8 cases) due to intercurrent disease.

TABLE 10

MORTALITY UNDER MEDICAL OBSERVATION

Cause of Death	No. of Cases
M n g t	1
Coronary Disease	3
Cerebral Vascular accident	[illegible]
Brain Tumor	1
Steroid Ulcer with fatal hemorrhage	1
Malnutrition due to ileitis	8
Total	16

Considering that the follow up of these individuals extended over a period of from 1 to 25 years (table 9) it will be seen that only 8 of the 542 cases died of the disease itself the remaining fatalities being attributable either to surgical intervention or to causes foreign and not directly attributable to the pathologic intestinal process

Chapter II Medical Therapy, Conservative Palliative Treatment of Regional Ileitis

General Directions

THE PHYSICIAN should direct his patients to adhere to the following regimen

Live in an atmosphere which is peaceful Try to control anxiety worry or mental upset Plan every day so as to have a rest period and as much quiet as possible

Fresh air and sunshine are fine aids to a quick recovery

No competitive games or strenuous exercise Plan recreation which does not produce nervous tension or great fatigue no tennis match no card games for money no horse back riding

Have a full and highly nutritious diet by eating three regular meals plus light mid morning mid afternoon and evening lunch That is eat *once every two and a half hours* throughout the day and little or nothing *after* 10 p m

Diet

A bland low fat protein rich diet should be instituted Abundant proteins and the liberal use of carbohydrates are necessary to maintain nutrition against the wasting of the disease and against hypoproteinemia that may ensue as a result of protracted fever and diarrhea Coarse fruits and vegetables should be eliminated soft vegetables well cooked should be pureed or passed through a collander Fruit juice may be allowed in limited quantities soft fruits such as bananas apple sauce soft pears and ripe peaches are allowable The greatest attention is paid to meats and fishes cheese protein milk and eggs as food with high nitrogen content The diet should be supplemented by the administration of protein casein hydrolysate or sustagen with high amino acid content 6 8 or 12 ounces a day taken in milk water fruit juice cocoa substitutes or in any manner that makes them palatable

In one case of high ileo-jejunitis where operation was contra

indicated a gain of 50 pounds of weight and a return to fair health and strength followed a conscientious forced attempt at superalimentation with protein foods and amino acid commercial preparations

Foods Allowed in Diarrhea

Milk At least a pint a day Milk need not be boiled Cultured milks may be used acidophilus buttermilk etc Mellin s food or malted milk may be added to milk *Note* Most persons tolerate milk very well However milk may cause diarrhea in those few persons who are allergic to it in such instances the milk should be omitted

Eggs Two or three daily Use in any form except raw or soft boiled

Cheese Any mild cheese may be used cottage pot or sour cream cheese gruyere swiss etc Small portions of sour cream are permissible

Cereals All highly milled grains that are well cooked farina cream of wheat Wheatina cornmeal white rice Ralston etc *Note* When using ready to serve cereals check advertising and reject all cereals containing *bran* Safe ready to serve cereals are Cerevin corn flakes grapenut flakes pablum puffed rice puffed wheat Spaghetti noodles and macaroni in moderation

Meats All leans meats boiled baked or broiled ground lean steak roast beef steak liver of all kinds veal lamb smoked ham chicken squabs turkey

Fish All white fish boiled baked or broiled halibut cod flounder sea bass etc shell fish oysters and clams

Bread White bread (not too fresh) melba toast swieback rolls plain sweet breads like brioche also crackers made of white flour

Butter In moderation Thin sweet cream if well tolerated

Fruits With the exception of orange juice and ripe bananas all fruits must be cooked or sieved Use apple sauce pears peaches prune apricots etc

Vegetables Use tomato juice Sweet or white potatoes cooked any way but fried Carrots green pea string beans onions spinach beet turnips tomatoes should be cooked and pressed through a sieve In milder cases cooked chopped spinach and beet tops asparagus tips and fresh tender lettuce may be used Canned infant foods are very satis factory for use

Desserts Custards Bavarian cream blanc mange bread rice and

tapioca puddings fruit whip gelatin jellies plain sponge and angel cake plain cookies Ices and ice cream are not desirable but may be used in moderation in mild cases

Miscellaneous Strained jams and preserves may be used in limited amounts grape pear apricot and pineapple juices may be used in small portion Juices of all mild cooked fruits may be used with added Dextri Maltose (not lactose which is laxative) Hard candies are to be encouraged

A certain amount of seasoning is allowable that is salt and pepper in moderation except during steroid therapy

Foods to Avoid During Diarrhea

1 Avoid all raw fruits and vegetables except strained orange juice in small amounts and ripe bananas All other fruits should be stewed

2 Avoid bran in (a) coarse breads (pumpernickel whole wheat bread muffins health breads etc) (b) coarse cracker (whole wheat rye crisp swedish wafers etc) (c) coarse cereal (oatmeal brown rice barley hominy pettijohn etc) Dry cereals are allowed

3 Avoid any gas forming food such as cabbage corn kholrabi broccoli pickles and reli hes of all kinds also skins of baked apples and potatoe Eat no beans peas or lentil except in pureed form

4 Avoid nuts raisins coconuts figs dates etc even if used in small amounts in puddings or cookies

5 Avoid heavy fat foods gravies sausages pa tries doughnuts fried meats and fish

6 All condiments especially pepper mustard horseradish vinegar etc are best avoided Therefore do not use any highly seasoned and spiced foods such as smoked meats and fish frankfurters most canned meats and fish salt fish olives etc

7 Avoid fish high in fat—salmon shad etc and shellfish shrimp lobster and crab

8 Avoid all grossly sweet foods preserves most candies all rich cakes with icings and fillings

9 Care must be taken not to use certain foods which are laxative e g large amount of lemon grapefruit or orange juice raw vegetable juices long iced drinks and many cups of too hot drinks as well as melons grapes plums mola es raw or soft boiled eggs

Following is the diet suggested for diarrheal disea es

Sample Menu

8 00 a m *Breakfast*

Orange or tomato juice ½ cup (dilute with water if preferred) Cereal with milk and sugar Bread (white) 2 slices (toasted) with butter Egg (1 or 2) boiled hard poached shirred or scrambled Milk cocoa or weak tea (1 cup)

10 30 a m

Hard boiled egg and cracker and milk cocoa or weak tea and cracker

1 00 p m *Lunch or Supper*

Choice of soup strained dried bean or split pea soup or cream soup (made with strained vegetables) or broth and any other strained soup

Choice of main dish Eggs or macaroni and cheese or portion of liver meat or fish

Serving of potatoes rice or noodles Bread (white) 2 slice with butter

Dessert Strained cooked fruit plain cake or custard

3 30 p m

Banana or ½ cup orange or tomato juice (see 10 30 a m)

6 30 p m *Dinner*

Choice of soup

Choice of main dish Lean beef (boil broil or roast) chicken turkey or fish Portion of strained cooked vegetable Portion of potato rice or spaghetti *Bread or roll with butter or jelly*

Dessert Jello corn tarch pudding or apple sauce Milk cocoa or weak tea

9 30 p m

Milk soft drinks may be taken in small quantities if not too cold and most of fizz is expelled (or see 10 30 a m and 3 30 p m)

Ambulation

Since most cases of regional ileitis are afebrile patients may be allowed some physical activity They are best treated as ambulant cases because the long course of the disease would make persistent insistence upon bed rest a psychic and mental handicap Most of the patients suffering from ileitis are not strong enough to work or attend higher educational schools or colleges but they are happier up and about and would probably gain little from prolonged bed rest Psychologically these patients are better when actively employed and busy invalidism or semi invalidism should thus be avoided Adolescents should be encouraged to read and continue their education even when confined to home The acute cases and those with a febrile course should have bed rest during the active phase thereafter early ambulation is advisable to preserve muscle tone (Femoral phlebitis and pulmonary embolism have not been noted in any cases in this series)

Various Medications

In dehydration particularly with diffuse draining fistula water and electrolyte replacement is best attained by the use of parenteral intravenous therapy Saline solution Ringer s solution 5 per cent glucose in water or in saline are indicated in amounts of 1500 cc per day or 100 to 150 gram of protein daily Blood plasma and occasional transfusions of 500 cc are indicated for protein replacement and in instances of advanced anemia

In chronic ileitis vitamin replacement is strongly indicated Concentrates of vitamin B complex reinforced by thiamin 10 or 20 milligrams per day may be administered orally although the absorption in the face of diarrhea may be problematic In all cases intramuscular injection of crude liver extract and of vitamin B complex 2 cc of each should be given into the buttock every other day Vitamin B_{12} in doses of 50 to 100 micrograms should be added in cases of severe anemia as well as iron by mouth It is rare that the other vitamins are indicated there is no material deficit of vitamin A or carotene nor of ascorbic acid nor of vitamin D in instances of ileitis since the diarrhea is rarely so profound as to create such vitamin deficiencies except after extensive and repeated surgical resection or short-circuiting procedures Synthetic vitamin K is indicated however in all instances of hemorrhage from the bowel wall even though the prothrombin time is well within the normal range Five to fifty milligrams of synthetic vitamin K daily intramuscularly or by mouth should as in ulcerative colitis control the hemorrhagic manifestations

The insoluble sulfonamides are indicated in regional ileitis, even though the therapeutic result has not been convincingly demonstrated Whether the disease is bacterial in origin or nature has not been demonstrated But the bacterial contamination of the intestinal ulcerations and some of the suppurative complications call for antibiotics that would tend to sterilize the bacterial content of the intestinal lumen Some efficacy of the sulfonamides in controlling the symptoms and progression of the disease seems suggested in studies of the use of sulfasuxidine and sulfathalidine (Crohn) in ileitis though convincing proof is lacking and these drugs in the largest percentage of cases fail to accomplish any striking therapeutic result Sulfasuxidine (succinyl-sulfathiazole) in doses of 0 25 gram per kilogram of weight is frequently employed the usual method is an initial dose of approximately 20 to 36 half gram

tablets (10 18 grams) followed by dosage of 5 to 9 tablets four times daily by oral administration Sulfathalidine (phthalylsulfathiazole) 0 1 gram per kilogram of weight usually 3 to 6 half gram tablet daily are equally efficient

Both of these drugs are bland and relatively free of untoward results Agranulocytosis has not been observed in thi series nor has hepatitis been seen except in one instance

Penicillin has no apparent specific effect on ileitis though it is useful in controlling the suppurative complications when walled off perforation does occur As a preoperative and postoperative antibiotic form of therapy penicillin is in great favor with most surgeons Streptomycin too when given intramuscularly 2 grams daily in divided six hour doses and one gram orally coincidentally may sterilize the intestinal tract and produce a sterile culture of the feces It is questionable however whether streptomycin has any clear indications for its use in the chronic protracted form of ileitis

Many of the broad spectrum antibotics are useful in cases of regional ileitis particularly in the presence of suppurative complications Aureomycin and terramycin because of their side effect in suppressing the normal bacterial flora of the intestinal tract are to my mind contraindicated Chloromycetin is very useful as well as achromycin in 250 to 500 milli gram dosage three times daily the newer Mysteclin has a wide range of anti bacterial action without unduly disturbing the intestinal flora and tends to combat the overgrowth of staphylococci and monilia in the feces

As regards steroid therapy the enthusiasm in the prompt some times spectacular effect of the steroids a employed in ulcerative colitis cannot be transferred in an equal degree to the treatment of regional ileitis Occasional early reports are beginning to appear in the literature demonstrating favorable effects of ACTH and the cortisones in enteritis but it is still too early to draw conclusions (Gray et al [3]) The steroids—hydrocortone cortisone or prednisone—are best given by mouth in dosage up to 15 to 30 milligrams daily Their effect is to improve appetite and well being and reduce fever they have little effect on the diarrheal manifestations An abdominal mass with fistulous inter communications and skip lesion is not likely to be cured by the steroids but their tendency to throw the patient into a remis ion of his active symptoms is valuable In higher ileo jejunitis large or massive do es of steroids by mouth (hydrocortone) or ACTH by injection

(Acthar Gel or Cortrophin Zinc) have a decidedly beneficial effect and encourage or encompass such healing as is only possible in the upper segments of the involved small intestine The Cushing syndrome occurs rarely intestinal perforation never (Sayer Brown and Dearing Stanley Rosenberg and Cleroux)

Radiation therapy has been rather extensively employed it was originally invoked by Eggers for the control of cases of intestinal granulomas and has been recommended and used by many writers in the literature Our own experience with radiotherapy in ileitis has been very disappointing though it has been limited to few cases We have observed the use of extensive radiotherapy in 18 cases the radiation therapy having been previously employed by clinicians in attempts to control the disease and its complications Those cases that we have seen have all been failures If there have been successes in the use of radiotherapy in ileitis they were not apparent in this series under study nor when employed by us as an initial form of therapy Bopp Bargen and Dixon reported in 1950 the findings of the Mayo Clinic in 50 patients treated by roentgen therapy In 20 of 43 patients so treated the results were very favorable the patients became symptom free and were able to return to their former occupations Fourteen others were improved 7 were not helped and 2 had died

In instances of intestinal obstruction the Miller Abbott Harris or Cantor tube is beneficially employed and by decompressing the intestinal lumen produces amelioration of the obstructive phenomena

tablets (10 18 grams) followed by dosage of 5 to 9 tablets four time daily by oral administration Sulfathalidine (phthalylsulfathiazole) 0 1 gram per kilogram of weight usually 3 to 6 half gram tablets daily are equally efficient

Both of these drugs are bland and relatively free of untoward results Agranulocytosis has not been observed in this series nor has hepatitis been seen except in one instance

Penicillin has no apparent specific effect on ileitis though it is useful in controlling the suppurative complications when walled-off perforation does occur As a preoperative and postoperative antibiotic form of therapy penicillin is in great favor with most surgeons Streptomycin too when given intramuscularly 2 grams daily in divided six hour dose and one gram orally coincidentally may sterilize the intestinal tract and produce a sterile culture of the feces It is questionable however whether streptomycin has any clear indications for its use in the chronic pro tracted form of ileitis

Many of the broad spectrum antibiotics are useful in cases of regional ileitis particularly in the presence of suppurative complications Aureomycin and terramycin because of their side effect in suppressing the normal bacterial flora of the intestinal tract are to my mind contraindicated Chloromycetin is very useful as well as achromycin in 250 to 500 milli gram dosage three times daily the newer Mysteclin has a wide range of anti bacterial action without unduly disturbing the intestinal flora and tends to combat the overgrowth of staphylococci and monilia in the feces

As regard steroid therapy the enthusiasm in the prompt some times spectacular effect of the steroids a employed in ulcerative colitis cannot be transferred in an equal degree to the treatment of regional ileitis Occasional early reports are beginning to appear in the literature demonstrating favorable effects of ACTH and the cortisones in enteritis but it is still too early to draw conclusions (Gray et al [187]) The steroids—hydrocortone cortisone or prednisone—are best given by mouth in dosage up to 15 to 30 milligrams daily Their effect is to improve appetite and well being and reduce fever they have little effect on the diarrheal manifestation An abdominal mass with fistulous inter communications and skip le ions is not likely to be cured by the steroids but their tendency to throw the patient into a remission of his active symptoms is valuable In higher ileo jejunitis large or massive doses of steroids by mouth (hydrocortone) or ACTH by injection

di ease which represents healing with scarring and constriction of the lumen of the bowel Occasional partial obstruction suggests the lighting up of a previou ly quiescent lesion here the edema of the bowel wall causes constriction Localized short circuiting procedures are clearly indicated since decompression of the dilated segment of the proximal bowel is usually protracted cumbersome and only temporarily satisfactory

6 *Recurrent Ileitis* While most recurrences lend themselves to medical conservative therapy a persistent active recurrence with renewed fistulous tracts hemorrhage or obstruction necessitates a new surgical approach

7 *Perforation* Free perforation with peritonitis is rare exceedingly so walled off perforations are common When this occurs with sealed off abscess formation the purulent cavity must be drained at least and the original disease attacked if such can be accomplished without inviting generalized intraperitoneal infection

Contraindications for Surgical Intervention

1 Diffuse ileitis or ileo jejunitis with involvement of so extensive an area that the sacrifice of the disea ed segments would endanger nutrition and invite electrolyte imbalance

2 Ca es of so-called mucosal type in which the lesion instead of remaining stationary shows a progressive tendency to extend orally and invade new proximal segments of the ileum and jejunum

3 Acute ileitis Knowingly to enter the abdomen in the presence of an acute febrile rigid abdomen is to invite disaster and to chance a high mortality rate

4 Ca e of combined ileo-coliti in which both ileum and some segment of the colon are synchronously involved While surgical intervention i eventually u ually a necessity in this complicated form of two combined di ease surgical interference should be undertaken only after long and eriou thought has been given to the type of procedure to be followed

The T ming of the Surgical Attack

The increasing con ciousness of the high percentage of recurrences after operation ha led to much pessimi m regarding the surgical end result The pendulum has of late swung far to the right probably too much so as will be seen shortly in a review of the end results of our

Chapter 12 Indications for Surgical Intervention in Regional Ileitis

OPERATIVE INTERFERENCE is indicated in regional ileitis under certain given conditions

1 *The chronic localized form of the disease* usually involving the terminal segment of the small bowel which over a long period of time remains static and shows no tendency to spread A mass is usually palpable in the lower right quadrant of the abdomen internal fistulous tracts are demonstrable on the roentgen films fever secondary anemia exist The mass itself *constitutes an indication for operation since it means many loops involved with intercommunicating fistulous tracts* such masses rarely heal spontaneously

2 *Fistulas* to the abdominal wall These fistulas originate in a diseased segment of bowel indicating persistent and active disease at the base of the fistula and do not heal without some surgical procedure that removes or short circuits the basic lesion

3 *Perirectal Fistulas* These fistulas precede accompany or follow active suppurative disease higher up *They do not heal spontaneously* but require a surgical attack upon the original focus in the intestine above *Operation upon such perirectal fistulas without first attacking* the original focus is fraught with disappointment and much discomfort and invalidism to the patient The loss of a tonic rectal sphincter leaving a patulous anus without control in the presence of diarrhea constitutes a most disastrous situation

4 *Hemorrhage* occurred in 25 instances either as an initial or as a late complication of the disease Gross bleeding occurs particularly in the postoperative cases *with manifest recurrence proximal to the anastomosis* The hemorrhage may take the usual form of melaena but hematemesis is not uncommon While acute hemorrhage may and usually does subside spontaneously persistent bleeding constitutes an indication for surgical intervention

5 *Intestinal Obstruction* Usually a late manifestation of the

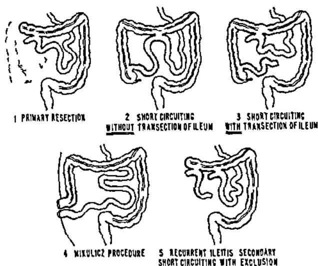


Fig 58a Types of operative procedure

forture In most instances the failure to transect the ileum above the upper pathologic limit of disease is accompanied by persistence of symp toms now a simple transection of the ileum constitutes a curative procedure [1 3]

The type of anastomosis of ileum to colon varies with the individual surgeon We prefer the side to side method of anastomosis some surgeons carry out end to side ileo colostomy thus avoiding a blind loop The blind loop in the experience of our surgeons rarely gives trouble but has been known to create severe secondary anemias to be the source of late gross hemorrhage and occasionally to cause obstruction or proximal dilatation The side to side anastomosis can be accompli hed with greater facility and with le s risk of leakage and is most satisfactory

own more extended series of operated cases Perhaps the fault lay in the timing of the surgical procedure Some authors including ourselves thought that radical intervention was indicated as soon as the diagnosis was established The disappointing late returns created a warrantable atmosphere of caution Perhaps if the surgical approach were better timed the end results would be more favorable If operation were delayed until the inflammatory process cooled off and healing resolution were begun the resection or short circuiting would be more successful because among other factors the upper limit of the disease would be more easily recognized at the time of operation On the other hand too much marching time and procrastination may prolong the debilitating aspects of the disease and leave the patient in an atmosphere of suspense and doubt emphasizing the psychic aspects of the illness

The best time to operate is when medical conservative treatment antibiotics steroids and rest have been exhausted without avail and after due process of care This is probably during the second or third year of the illness (see table 13) the follow up of such cases shows the greatest percentage of surgical cures over a long period of time

Type of Operative Procedures

To a large extent both in thi country and throughout the world according to the literature a short circuiting procedure usually in the form of an ileo transverse colostomy *with transection of the ileum* is the *procedure of choice Certainly it is in our institution the Mount Sinai* Hospital where resections are rarely performed On the other hand primary resection holds promise in the hands of many schools of merit and experience and has many enthusiastic followers The palliative short circuiting procedure can be accompli hed with practically no operative mortality [124] Primary resection previou ly was accompanied by an opera tive mortality of 12 to 15 per cent but has now according to Van Patter et al at the Mayo Clinic been reduced to 2 3 per cent The recurrence rate after either procedure is material but favors the short circuiting operation which is a sociated with a definitely lower rate of recurrent disease Since the operative risk is lesser or nil for the short circuiting procedure and the rate of recurrence is less it seems difficult to justify resection as the operation of choice

In any event tran ection of the ileum high above the lesion at least 12 to 18 inches is mandatory although even that primary essential maxim is not universally accepted much to our surpri e and discom

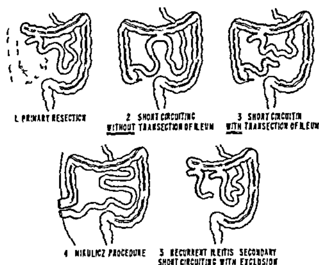


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Chapter 13 Surgical Treatment of Chronic Regional Ileitis Historical Survey

THE SURGICAL RELIEF of regional ileitis is indeed a complicated and changing picture It is very *interesting to follow chronologically* the trends of opinion over the last 25 years and to note the various schools of thought and procedure The subject is apparently still in a state of flux as is natural when methods change procedures differ, judgments do not agree and the follow up period is all too short

In general one may note historically certain salient or outstanding surgical procedures in the passing years of experience

1 Resection in one stage was the initial procedure of choice

2 The gradual evolution of a two stage procedure (short circuiting followed subsequently by resection of the original lesion)

3 Adoption of a single stage operation namely ileo transverse colostomy with transection of the ileum as a sufficient procedure to induce cure

4 Preference for primary resection by the Lahey Clinic

5 Advocacy of a two stage operation by the group at the Mayo Clinic

6 Growing realization of the increasing incidence of recurrences following all types of surgical interference

These six stages are described in detail below

The initial surgical historical procedure at Mount Sinai Hospital practiced by A A Berg was primary resection carried out on the first 14 cases of terminal ileitis this series was increased to 32 instances of resection by Berg in 1936 Correspondingly most of the early cases in the literature concerned themselves only with primary resections of the terminal ileum In 1936 Koster reviewing 100 operated cases from the literature found resection almost universally carried out as the procedure of choice In 1939 Ravdin and Johnston reviewing the surgical literature found 290 instances of primary resection against only 88 instances of short-circuiting procedures

By 1933 we had the suggestion made independently by Clute and by Homans and Hass of ileo transverse colostomy that is short-circuiting of the lesion as a sufficient procedure rather than resection Unfortunately neither contribution mentioned whether transection of the ileum proximal to the lesion had been performed Even before this date Estes and Holm had warned against such a procedure they demonstrated in 2 human cases and by animal experimentation that huge dilatation of the sidetracked and excluded loop of ileum could and did occur This point of view however was subsequently contradicted by the studies of Ginzburg Colp and Sussman By surgical experience substantiated by careful roentgenologic studies these latter authors proved that a short circuiting procedure with transection of the ileum was a safe and satisfactory procedure that involved no complication from the excluded loop of ileum

By 1934 some of the members of the Mayo group (Clark and Dixon) were already experimenting with short circuiting procedures having utilized such a plan in 5 cases out of 13 operables Again transection of the ileum was not mentioned In 1939 Clark and Dixon suggested for the early stages of the disease a simple short circuiting procedure with transection of the ileum which carries a low mortality and provides an opportunity for the diseased segment of the bowel to improve by being placed at rest Subsequent resection of the diseased area was utilized if activity of the original site of the disease continued If the disease process was far advanced primary resection a radical extirpation of the diseased segment was advocated

In 1936 Koster for the first time warned that if a short circuiting procedure is to be performed transection or occlusion of the ileum must be carried out he still preferred primary resection since he suspected the undesirability of leaving in situ the original focus of infection

The importance of transecting the ileum above the diseased segment was realized in the following case in this present series

Case H S (Serial No 146) Male age 21 years For 18 months this young man had suffered with diarrhea fever and abdominal cramps A mass had formed in the right lower abdominal quadrant He had been operated on at that time and a short-circuiting procedure had been carried out without transection of the ileum Diarrhea persisted there was a weight loss of 30 pounds edema of the lower extremities was present due to hypoproteinemia. Clubbing of the fingers and severe secondary anemia (hemoglobin 62 per cent) were evident At operation a transection of the ileum above the point of and residual ileitis was the only procedure performed This was followed by a regain of the

50 pounds of weight lost and a subsidence of the peripheral edema of *the lower extremities Unfortunately two years later a recurrent ileitis* proximal to the old anastomosis was capable of demonstration a two stage resection of the recurrent ileitis resulted in cure

The transition of the Mount Sinai group from primary one stage resection to two stage resection and finally to a short circuiting procedure only is interesting to observe In 1936 though primary resection seemed to be in favor it was noted that both Lewisohn and Colp had 6 cases of short circuiting procedures with good results Lewisohn later (1938) reported 9 cases of short-circuiting or two stage procedures with only one death He again strongly emphasized that a lateral anastomosis between upper healthy ileum and the colon without transection of the ileum above the diseased segment is a useless operation since the affected part of the bowel is not put at rest

In one fatal case a primary ileo transverse colostomy with transection of the ileum had been *primarily performed After* a sufficient interval of what was then regarded as the proper sequence the second operation of resection of the primary residual focus of disease was carried out The resected specimen was now fully healed and cicatrized Unfortunately the child died postoperatively of pulmonary embolism due to an old rheumatic endocarditis The tragic death and the evidence that the secondary intestinal resection had been superfluous led to a revision of the views regarding the needs of the secondary resection Bowen and Day report the postmortem findings in a case of regional ileitis 9 years after symptomatic recovery following ileo colostomy The ileum previously affected was at the autopsy shown to be fibrosed and sclerotic the lumen almost obliterated by stenosis and by multiple adhesions Complete healing of the ileum had been affected by the short circuiting procedure

In 1939 Ginzburg Colp and Sussman published 14 cases of short circuiting operations for ileitis transection of the ileum being regularly carried out Again they were convinced of the lack of necessity for any subsequent resection the initial lesion drying up and undergoing atrophy after the short circuiting fistulae disappearing abdominal masses resolving The x ray studies of Sussman convincingly demonstrated no trapping in the excluded loop and good intestinal function through the new stoma

In 1941 Colp and Ginzburg published a report of ileo colostomy with exclusion as practiced in 22 cases of terminal ileitis with no deaths

3 of the series showed recurrent symptoms. Four of the cases were reexplored because of persistent diarrhea; in all 4 healing of the original site of infection in the terminal ileum was clearly demonstrable and no further resection was attempted. Six cases had abdominal wall fecal fistulas before operation; after the short circuiting procedure 5 of the fistulas healed and ceased to discharge content. In 1942 Ginzburg and Garlock published 54 cases of ileo colostomy with exclusion with no operative mortality. There were 2 recurrences of the disease in the proximal ileum and 5 cases with persistent clinical symptoms. Contrasted with this were 23 cases of primary resections with 4 deaths and 3 recurrences.

In 1945 a larger group of cases from the Mount Sinai Hospital was published (Garlock and Crohn) covering a 12 year experience with the surgical treatment of chronic regional ileitis. The series comprised 164 cases of enteritis, terminal ileitis and combined ileo colitis, most of which had been operated on by various surgeons in that institution (137 cases); the remaining 27 cases had been operated on elsewhere but reported for observation because of persisting symptoms. The inclusion of these latter cases, which represent failures of previous procedures, depresses the statistical value of the total end results of the series but had been included nevertheless in the interests of scientific accuracy. The results may be seen in table 11.

TABLE 11

SURGICAL TREATMENT OF CHRONIC REGIONAL ILEITIS

	Number	Deaths	Recurrences
Ileo-colostomy with exclusion	65	0	9 (13.8%)
One stage resection	55	9 (16.3%)	9 (19.5%)
Two stage resection	25	3 (12%)	8 (36.3%)
Combined ileo colitis	19	2 (10.5%)	3 (17.6%)

By a process of comparison the advantages of the ileocolostomy with exclusion are obvious. The mortality rate was nil, the recurrence rate (as of that date) was moderate but yet considerable. The group of cases comprising primary resection was less satisfactory; a considerable mortality rate was apparent, nor did there appear to be any compensation for the greater risk since the recurrence rate of resection was even greater than that of the exclusion operation. Here the longer follow up period of the earlier resected cases may well be a factor since recurrences were noted once 8 years and once 12 years after the original operation.

the intervening years having been a period of apparent perfect health Bockus had already noted a recurrence of postoperative ileitis 9 years after apparent good health

The two stage operation consisting of a primary ileo colostomy with transection of the ileum followed some time later by a resection of the primary focus of disease constituted the most distressing group and naturally so because these cases all represent failures of short circuiting procedures the second stage of the operation was forced by the *gravity of the persisting symptoms at the original site of disease Actually* they represented failures of the first stage short circuiting procedure The forced secondary operation was fraught with a moderate mortality (12 0 per cent) but failed to result in amelioration of symptoms or relief in 36 3 per cent of this smaller series

The Lahey Clinic favored a Mikulicz type of resection for ileitis the diseased ileum and the ascending colon are brought out on the surface of the abdomen exteriorized and resected extraperitoneally A secondary closure of the entero tomies is later performed Marshall in 1940 and again in 1943 reported a ten year survey of 55 patients surgically treated The operative mortality was 5 5 per cent in a follow up that covered 42 patients of the series there were 5 recurrences or 9 6 per cent

Of this series 35 cases underwent the Mikulicz procedure with but one death a highly commendable record

The group at the Mayo Clinic seem to prefer a two stage operation In 1937 Pemberton and Brown reported 39 cases of ileitis treated by two stage short-circuiting and resection with 3 deaths They allowed 3 weeks to 6 months between the first and the second procedure Transection of the ileum as part of the first operation was always mandatory In 1938 Dixon reported 40 operative cases the procedures were evenly divided between primary resection two-stage operations and short circuiting alone Again the gross mortality was low 10 per cent

In 1941 Mayo and Judd reported a full 100 cases 64 of which underwent the two stage operation with a 3 per cent mortality the average length of time between the two stages was 14 4 months With multiple procedures in the complicated cases Brown and Donald had a higher mortality of 9 per cent for a larger series (178 cases) They suggest surgical removal of the diseased segment of bowel a two-stage procedure is better than a one stage operation

The most disappointing effects are seen when attempts have been made to perform resections of the ileum in continuity with end to end anastomosis of the small bowel Procedures such as this one are insufficient unphysiologic and lead to skepticism (3 such cases in the present group) This same criticism does not apply to high jejunal involvement where local resection is eminently successful

In 1938 Dennis suggested vagotomy as a possible cure for ulcerative colitis or regional enteritis the idea has never proved to be useful but deserves consideration

Chapter 14 A Review of Our Own Experience With Operative Procedures for Regional Ileitis

OF OUR SERIES of over 500 cases of regional ileitis 385 were subjected to surgical intervention at our instance or were or had been operated on elsewhere the indications for and the timing of the operation having been set by internists and surgeons at other institutions

The main question of surgical interference revolves about one basic question namely which is the better procedure short circuiting or resection? Which of these two procedures is accompanied by the lower operative mortality rate? Which gives the best results as viewed from late follow up studies? What actually is the true figure for recurrences of the disease after either or both of these attempts to cure or to eradicate the primary seat of the disease?

TABLE 12

TYPES OF OPERATIONS FOR ILEITIS AND END RESULTS

General Total 385 cases

		Good	*Recurrences*	*Deaths*
Short circuiting	232 cases	—157 (67 6%)	67 (29%)	8 (3 4%)
Resections	116	— 67 (57 8%)	38 (32 7%)	11 (9 5%)

Lost to follow up 37 cases

Many of the cases in this general group were not our responsibility since they had been operated on elsewhere This over all series might well have been loaded with the failures of others since our office and those of large institutions all become repositories of disappointed failures We therefore separated our own series of cases i e patient in whom the original diagnosis had been established by ourselves in which we set the indications for and the timing of operation and supervised the postoperative course In addition the personal follow up over succeeding years was more complete and more prolonged A comparsion of our Primary Group those cases in which we had sole responsibility with those operated on elsewhere should be interesting

TABLE 13

Primary Group—Follow-up Operative Results

		Good Results	Recurrences	Deaths (later)
Short circuiting	125 cases	—86 (68.8%)	34 (27.2%)	5 (4%)
Resection	6	—39 (63%)	17 (27.4%)	6 (9.6%)

Foreign Group—Follow-up

		Good Results	Recurrences	Deaths (Operative and later)
Short circuiting	107 cases	—71 (66.3%)	33 (30.8%)	3 (2.9%)
Resect	54	—28 (51.9%)	1 (39%)	5 (9.1%)

Lost to follow-up in both series 37 cases

The differences between the two groups is not great

1 As to choice of operation in both groups twice as many short circuiting procedures were carried out as were resections

2 Operative mortality for the primary group was 11 out of 187 cases or 5.9 per cent There were 8 additional deaths during the follow up which covered 1.25 years The long view mortality for the short circuiting procedure was in the total group (table 11) 3.4 per cent as compared to resections which have a mortality rate of 9.5 per cent

The immediate operative mortality however is more significant Of the 12 deaths (in our Primary Group) directly following the surgical undertaking 9 followed resection only 1 a short circuiting procedure There was 1 accidental death in the operating room

Obviously the surgical risk attending resection is far greater than that of the by pass operation

3 The end results again favor the short circuiting procedure 67.7 per cent as against 57.8 per cent for cases which had undergone resection

4 By the same token the rate of recurrence for the short-circuiting was 29 per cent for resection 32.7 per cent (table 11)

All arguments favor the short circuiting in which the operative mortality is lower good results higher and the late recurrence rate distinctly lower Obviously too the recurrence rate is not as often quoted in the literature 35 40 50 or even 60 per cent but is by these figures roughly 30 per cent The 70 per cent of cases quoted as good are free of symptoms except for frequent mild diarrhea have regained weight been restored to good nutritional status do not exhibit anemia and are free of open fistulas Most if not all of this group have resumed their occupation and domestic activities many of the women have borne

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Fig 59 R c r ent l tis resect n f orig nal d e in ol ing lower ileum d an stomos s

the result of the longer periods of observations since recurrence are now observed to take place as late as 10 15 and even in one case 25 years after the initial procedure The full tory may not even now be told since it the average age of the ileiti patient i 27 6 years and the follow up is 25 years these individual are now perhap 52 years old and still may have two or three decades to live The next generation of clinicians and surgeon may still further alter this life hi tory of ileiti and the late surgical (and m dical) results

Recurrences after operation have been noted in the literature from the initiation of a surgical plan of attack (Homans and Hass Shearer and Jackson Oppenheimer Felg r and Schenk) but the e figures lik ours were usually quoted as about 15 per cent The more recent surgical literature is truly di couraging at the Lahey Clinic Mar hall and

children and the men are fertile Good results are checked by repeated radiographic examinations

5 The duration of the follow up observation and the timing of recurrences is important

TABLE 14

FOLLOW UP OF SURGICAL CASES

Short Circuiting—232 cases				*Resections* (Primary)—116 cases			
Years	*Good*	*Recurrences*	*Deaths*	*Years*	*Good*	*Recurrences*	*Deaths*
0 1	30	17		0 1	6	5	
2	26	14		2	10	6	
3	12	11		3	11	2	
4	11	5	8	4	5	4	11
5	11	3	Operative	5	3	2	Operative
5 10	28	12	and	5 10	15	11	and
10 15	30	3	Follow up	10 15	10	4	Follow up
15 20	8	2		15 20	5	3	
0 25	1	0		20 25	2	1	
25 30	0	0		25 30	0	0	
	157 (67 7%)	67 (29%)			67 (57 8%)	38 (32 8%)	

The follow up covered from 1 to 25 years it was not complete since 37 cases were lost to follow up Most of the cases classified as good had been followed for only 5 years but a good proportion over 40 per cent were observed over a period of 5 to 25 years and these maintained their good status with the passing of considerable more time this statement pertains to both types of operation

Recurrences

The recurrence rate in our series is roughly 30 per cent It will be noted from table 13 that most of these recurrences occurred within the first 3 years after operation Late recurrences are not infrequent and may be observed 5 15 and even 25 years after the surgical procedure During this intervening period the patients are well as judged by good nutrition and weight and restoration to living efficiency a mild diarrhea is not uncommon Most of these patients are checked at interval by radiographic studies Time seems to be a most important factor In 1945 a follow up of a series of 164 cases (Garlock and Crohn) at the Mount Sinai Hospital showed a recurrence rate of 13 8 and 19 5 per cent for exclusion and one stage resection respectively (table 11) By 1951 this rate was revised to a figure of 22 5 per cent and in 1957 to approximately 30 per cent It is obvious that these later corrections are

when anastomosed to a healthy colon should sooner or later develop a new recurrent disease If that particular segment of ileum had been left in place it would have remained free of disease for years Transposed to the colon it develops disease And thi i also true if a second or a third recurrence necessitate the duplication of the operative step Perhaps only a biochemical explanation will an wer thi riddle

It i also difficult to explain the rationale and method of propagation of such recurrence particularly when the operation had been performed by a competent surgeon one of experience in recognizing the highest pos ible skip-lesion In the best of hand where the tran ection isolating the ileal lesion ha been placed high and far di tant above any suspi ciou ly involved areas approximately 30 per cent of recurrences are conceded

Two possible method of propagation of the recurrences suggest themselves

(a) The surgeon i unable to recognize the uppermost skip-lesion and makes his anastomosis too low in the ileum That thi mi take is due to ignorance or inadvertence or inexperience is gainsaid by the fact that recurrence occur at the hand of the mo t careful meticulou and experienced surgeons and are frequently checked by biopsy of the small bowel at the time of operation Obviou ly if it i a mistake in judgment it occurs because the muco al or submucosal infiltration i so minimal a to preclude recognition by palpation or inspection of the wall of the small gut which i utilized for the ana tomosi It seem likely that such skip areas may and do escape the vigilance of even the mo t adept urgeon If thi i the explanation then the loop of ileum chosen for the anastomosi mu t be high and far away from any suspected pathologic involvement Such a high choice invites the danger of nutritional di turb ances by sacrificing too much muco a neces ary for food ab orption and by inviting the possibility of diarrhea

(b) The recurrence are due to the per i tence of a nidus of residual infection out ide the intestinal wall most likely in the retained and inflamed mesenteric lymph nodes If such were the case then recur rences hould occur with greater frequency after short-circuiting opera tions than after radical resection a fact which i contradicted by the table of figures In the radical excisions of the le ion it i u ual to remove the succulent enlarged lymph nodes with the mesentery and with the original lesion a deep angular resection of the mesentery being performed by most experienced surgeon However even with such a radical excision the recurrence rate (32 7 per cent) was higher than with short

Mathieson (1955) 30 per cent at the University of Pennsylvania Dyson Hodes and Rhoads (1954) 58 per cent at the Mayo Clinic Van Patter et al (1954) 54 5 to 66 per cent

The result of these discouraging late reports was to disparage the successes of surgery in regional ileitis it would seem to us that the pendulum has swung too far to the right and that the over conservative course of delay was often one of unnecessary procrastination and was not warranted by the most recent facts An operation that can give good results in 70 per cent of the cases and in which the recurrence may take place as late as 5 25 years after the surgical procedure is well worth while as a palliative procedure at least if not necessarily a permanent cure

Again the question arises as to what constitutes a recurrence The group at the University of Pennsylvania[99] suggest that a distinction exists between clinical and radiological recurrences The percentage of clinical is far below that of the so called radiological recurrences The radiologist studying the films of the new terminal ileum is often in doubt concerning the significance of slight irregularity in the mucosal outline of this segment of small bowel just proximal to the anastomosis Is this a natural irregularity in contour an operative artefact or does this uneven outline signify clinical recurrent disease?

Our own opinion is in agreement with those of the University of Pennsylvania group an irregularity of the new terminal ileum by radiography which has not previously been discerned is significant But if it is not accompanied by clinical symptoms of recurrent disease *the observation and its interpretation must be recorded and weighed* It may well be that the radiological demonstration precedes the onset of true clinical recurrent ileitis

These recurrences appear almost uniformly in the ileum just proximal to the anastomosis 6 to 8 inches in extent the pathology of the recurrence in the new terminal ileum grossly and histologically *resembling that of the initial lesion Skip lesion above the local recur*rence may extend continuously or in an interrupted fashion throughout the remaining ileum and even jejunum Internal (or external) fistula *frequently originate in the involved segment of recurrent ileitis* The recurrence is always in the ileum practically never in the colon even in the absence of any valvular structure the colon exposed for years to *recurrent ileitis seem to be immune to the disease* It is difficult to explain why a healthy ileum proved so by biopsy at the time of operation

permanent ileostomy above the recurrent lesion i the only means of saving life

The very rare involvement of the colon in recurrent ileitis is an interest ng negati e phenomenon for though there is no equivalent of an ileo cecal valve of Bauhin at the new anastomosis and though the recurrent ileitis empties unguardedly into the expo ed colon the natural immunity of the colonic muco a to the ileal infection seem to preserve it from involvement by extension This was impre sively demonstrated in one particular case an ileiti had been resected 18 years previou ly the nature of th lesion being little suspected Recurrence of symptoms took plac at the subsequent operation 18 years later the recurrent lesion and attached ascendin colon were re ected en masse the colon was free of disease though probably for most of the long period the recurrent ileitis emptied its content into th large bowel at the anastomo is

The Treatment of Recurrent Ileitis

Fortunately most of the recurrences are mild many of them ca i be controlled by con ervative medical treatment Such therapy consists of drugs that control the frequency of the diarrhea particularly the opiates and Kaolin preparations The anemia is treated by the intra mu cular injection of crude liver extract vitamin B complex 1 cc of each and B 50 to 100 micrograms every second day re t warm climate sunshine at the beach are very helpful An occasional case seem to be helped by radiotherapy sometimes too when emotional strains exist the help of a sympathetic and understanding p ychotherapist is welcomed

The insoluble sulfa compound sulfasuxidine or sulfath ilidine are often administered although their value is not proved The newer broad sp ctrum antibotics such a achromycin chloromycetin and Mysteclin are very u eful in the presence of infection fistula econdary abscesses and fever

The teroids are freely administered for recurrent ileiti as they are for the original disea e Here cortisone hydrocortone as in sprue case 20 m ll grams 3 to 4 t me daily or Meticorten predni one or prednisolone 5 milligrams 3 to 4 times daily by mouth The patients seem to do well on the steroids appetite weight and nutrition improve though a tru cure of the recu ent di ease is rarely demon trable

An increasing number of recurrences seem to do well they retain only mild cl nical symptoms under con ervati e care and this remains true for long period of follow up years Surgical intervention should

circuiting procedures (29 per cent) If the lymph nodes actually constitute the source of residual infection and reinfection it is necessary to postulate the spread against the normal lymphatic flow which is from the intestine to the lymph nodes rather than the reverse This is contrary to physiologic knowledge though retrograde reinfection and retrograde metastases do occur as in carcinoma Further it has been shown on secondary explorations after short circuiting procedures that when re examined the originally inflamed lymph nodes are now diminished in size and show retrogression of the infection

Diagnosis and Treatment of Recurrences

After the operation the patient usually regains weight and strength and appetite hemoglobin values improve fever ceases and diarrhea is absent or only relatively mild The diarrhea after operation may persist for a few weeks or up to six months but usually with time the defecation are reduced to two or three a day without pain or urgency

A recurrence of the disease is marked by a return of fever loss of weight increasing anemia and an exaggeration of the diarrhea The radiographic demonstration of irregularity of the mucosal pattern of the new terminal ileum narrowing of the lumen rigidity and distortion in the 6 to 8 inches of small bowel just proximal to the anastomosis confirm the existence of a recurrence (fig 49) The recurrence is best demonstrated by barium enema the possible involvement of a higher segment of small bowel must be established or excluded by the barium meal study of higher ileum and jejunum Many of these recurrences are exceedingly mild fever is absent loss of weight minimal diarrhea and anemia being the only presenting symptoms Even the diarrhea is undependable as a sign of recurrence since postoperative diarrhea even in successful operative cases is not unusual One depends therefore to a large extent upon the radiographic interpretation of the loop proximal to the anastomosis (fig 50) Such interpretation is not infallible just as the original radiographic diagnosis of a lesion in the terminal ileum is not always accurate errors of omission and commission being likely to occur

Recurrences with gross intestinal hemorrhage are rare with abdominal wall fistulation or internal fistulas they are somewhat more frequent Recurrences in the colon the rectum and the upper small intestine have been noted fortunately infrequently but they represent a sad picture since little of a further surgical nature can be attempted Sometimes

Secondary recurrences do occur fortunately infrequently These are usually met when the indications for surgery become mandatory by a third anastomosis usually an ileo sigmoidostomy again with transection of the ileum above the secondary recurrence These cases too though infrequent occasionally do well the diarrhea following such repeated surgery is not excessive

A somewhat discouraging report on secondary operations for recurrent ileitis is that of Kiefer at the Lahey Clinic in Boston Of 42 cases with one or multiple operations 27 were salvaged 10 were disabled 5 died

The more recent suggestion regarding treatment for extensive diffuse ileitis or ileo jejunitis comes from a Western group Vagotomy has been experimentally tried for the relief of symptoms and possibly the cure of severe ulcerative colitis The idea has been extended to cover also the possible very serious forms of ileo jejuniti Considering that a vagotomy is followed by atony when applied to the stomach it may well be that the putting at rest of the small intestine by the same surgical procedure can be similarly accomplished Certainly the idea is worth consideration (Dennis et al)

In cases under steroid therapy it is essential that at the time of operation the steroids should be stepped up rather than diminished Adrenal atrophy or insufficiency calls for renewed increased dosage before the operative procedure Electrolyte balance particularly sodium and potassium should be replaced when necessary and during the operation an additional booster dose of soluble cortisone (Cortef) should be administered in the intravenous infusion

be reserved for those cases only which represent failure under medical regimen and which develop complications such as fever abdominal wall or perirectal fistulas or where the recurrent pathologic process shows *an anatomical tendency to extend upward*

The surgical procedures for the cure of recurrent ileitis consist of a further short circuiting procedure usually an ileo transverse colostomy distal to the previous anastomosis again with transection of the intervening ileum so as to exclude the newly involved segment Some surgeon also transect the transverse colon distal to the first anastomosis bringing the proximal cut end out on the abdominal wall as a temporary or mucous colostomy A second stage procedure is now required to excise the recurrent ileitis and the attached transverse colon Other surgeons following the principle of short-circuiting merely make the new anastomosis transect the ileum so as to exclude the involved segment and make no attempt further to resect the recurrent lesion It is too soon to say which is the preferable surgical approach It is certainly true that one operation is always better than a two stage procedure provided it suffices to heal the recurrence The mortality of such operation for recurrent ileitis i exceedingly small and the improvement in well being weight and strength is very *satisfactory Unfortunately too many* instances can be cited of extensive and rapidly extending recurrences that defy surgical intervention Two such cases in this series will demonstrate the almost *malignant nature of the rapid and universal involvement of the small* bowel by recurrent ileitis

Case I M (Serial No 229) Male 17 years of age Si months of abdominal pain and diarrhea Regional ileitis involving the terminal 18 inches of the terminal ileum wa demonstrated radiographically and at the exploratory operation ileo transverse colostomy with exclusion of the ileum Recurrent symptoms occurred exactly one year later with rapid downhill cou e At exploratory laparotomy thirteen month after the original hort circ iting procedure a diffu leo jejunitis e tending up to the duodenum wa demon trated No further surgical procedure was attempted

Case I M (Serial No 110) Female single 29 yea s of age Eight years of alternating diar hea and const pation loss of 50 pound of weight Eleven months ago resection of terminal 2 feet of ileum (and ascending colon) for terminal or reg onal ileitis Six m nths later because of rap d recurrence of symptom *the patient again nderwent surgical exploration* The entire ileum p oximal to the ana tomo i and the jejunum were the seat of extensive recurrent inflammatory di ease Per stent abdominal wall fecal fistulas re ulted after the la t and fut le exploration The prognosis was absolutely hopeless

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Case 1 M (Serial No 229) Male 17 years of age Six months of abdominal pain and diarrhea Regional ileitis involving the terminal 18 24 inches of the terminal ileum was demonstrated radiographically and at the exploratory operation ileo transverse colostomy with exclusion of the ileum Recurrent symptoms occurred exactly one year later with rapid downhill course At exploratory laparotomy thirteen months after the original short circuiting procedure a diffuse ileo jejunitis extending up to the duodenum was demonstrated No further surgical procedure was attempted

Case 4 M (Serial No 110) Female single 29 years of age Eight years of alternating diarrhea and constipation loss of 50 pounds of weight Eleven months ago resection of terminal 2 feet of ileum (and ascending colon) for terminal or regional ileitis Six months later because of rapid recurrence of symptoms the patient again underwent surgical exploration The entire ileum proximal to the anastomosis and the jejunum were the seat of extensive recurrent inflammatory disease Persistent abdominal wall fecal fistulas resulted after the last and futile exploration The prognosis was absolutely hopeless

Warren and Sommer regard acute ileitis as rather common they cite a case reported by Erb and Farmer of a 2½ year old child who at autopsy showed peritoneal effusion marked edema of the ileum and colon closure of the ileo-cecal valve Peyer s patches and generally enlarged mesenteric lymph nodes But of 8 cases of acute ileitis which they themselves observed they regarded 5 as acute exacerbations of a previou ly existing chronic disease

In the 1949 edition of thi monograph we described 16 cases of acute ileitis The sex distribution was about equal the ages varied from 3½ to 37 years at the on et Many of the cases occurred in young children a fact which was confirmed in the current literature Thus the well described case of Erb and Farmer in a 2½ year old child with complete autopsy findings that of Harris in a 5 year old female child Schiff 1¾ years of age Warren and Sommers observed that the acute form of ileitis i more severe in young children since the diameter of the bowel is smaller and edema easily produces ob truction

Three of 8 cases reported by Meade occurred in children aged 6 8 and 9 years respectively Megret s case involved a child 3 years of age with successful resection of the involved ileum at the time of exploration Storrs and Hoekeman report acute ileitis in 8 children ranging in all from 3 months to 13 years

Our present or new series (1957) includes 15 cases observed since 1947 Of these 13 were males and 2 females a surpri ing reversal of our previous figures and seeming to point to a distinct predilection for the male sex The ages varied from 15 to 48 years giving an average age at onset of 28 years almost identical with that of our large series of chronic granulomatous ileitis (27 6 years)

In the present as in the past series the di ease is usually restricted to the terminal ileum the area of pathologic involvement extending from 4 to 18 inches in most cases in 2 of the present series at laparotomy the whole ileum was seen to be involved

Skip-le ions a seen in chronic ileitis are not mentioned by the operating urgeons an important observation since it is a clear indication of the fact that the primary seat of the disease is regularly at the terminal ileum the kip-lesion repre-enting a secondary and later exten ion in time and site The lesion at operation is characteri tic the terminal loop of ileum being bright red edematou soggy congested the mesentery thickened the lymph nodes enlarged in some cases not remarked in others In one case an abscess cavity was observed surrounding a per

Chapter 15 Acute Regional Ileitis

In the original description published in 1932 cases of acute regional ileitis were recognized and described The clinical picture was similar to that of acute appendicitis namely generalized abdominal colic pain tenderness over the right lower quadrant fever up to 101° or 102° F The white blood count was elevated A mass without active abscess formation was fairly constant At operation the findings were those of a mass of adherent and inflamed loops of ileum the terminal coil being red edematous soggy and brilliantly congested the mesentery of the gut was thickened and edematous and contained enlarged inflamed mesenteric lymph nodes Clear or cloudy fluid in small amount was present in the peritoneal cavity In rare ca es an abscess cavity contain ing thick aqueous but not foul smelling pus was encountered A general statement was made that some cases were resolved without operative interference others passed transitionally into the chronic phase of the disease It was presumed that the acute was but one phase of the chronic disease The number of cases was too small and the follow up too recent to allow any scientific statements other than a description of the clinical and pathologic picture Jackman shortly thereafter reported 2 almost identical cases in which the acute picture of ileitis represented only a flare up of the proce s upon the basis of an old chronic inflammatory lesion in the terminal ileum Both cases were successfully resected Erb and Farmer reported 4 cases of acute ileo-colitis in children Meyer and Rosi described 8 cases of regional ileiti four of which were of the acute type 3 of these 4 acute ca es underwent spontaneous resolution Rockey de cribed a case of thickening of the terminal ileum apparently an acute regional ileitis in a child aged 5 years

The ample literature that followed from the publications of many surgeons Clute Ladd Harris Bell and Brunn and our own pre ent group in this series amply bore out the facts as set down in the earlier publication Sufficient time experience and follow up have now elapsed to warrant a more complete clinical picture to elaborate upon the life cycle and prognosis of such case The surgical attack upon acute ileiti ha pa sed through several phase and may now be recapitulated in its pre ent and probably its final formulation



Fig 60 Acute ileitis 10 days after onset temperature 105 F at onset

logic survey corresponds almost identically to that seen at operation (fig 60)

The diagnosis concerns itself practically with the differentiation of acute ileitis from acute appendicitis The one and only possible clue lies in the presence or absence of diarrhea since as a rule ileitis is accompanied by diarrhea (14 out of 15 cases) and appendicitis by constipation Unfortunately both symptom complexes afford exceptions to the rule Ileitis may be accompanied by constipation though rarely (once only in this series) while acute appendicitis may occur with and in the presence of diarrhea To all intents and purposes however appendicitis

foration of the terminal loop of ileum the abscess containing fresh pus The serosa of the ileum is covered by a serofibrinous exudate free fluid being seen in the peritoneal cavity The pathologic or histologic findings in acute ileitis are almost identical to those of chronic ileitis A greater degree of edema is present leukocytic invasion is more prominent The villi show loss of epithelium and become mere shadows Very little slough of tissue is to be noted The serosa is edematous the blood vessels tremendously engorged The lymph nodes are extremely edematous with marked hyperplasia of the germinal centers (Harris)

The *clinical manifestations of acute ileitis show little variation* The onset of symptoms varies from one to 3 days in most cases extending up to 5 weeks The acute often fulminating onset is characterized by pain in the general abdomen or in the right lower quadrant the pain colicky in nature present in all cases accompanied by fever ranging from 100 to 103 F the curve being constantly elevated and not remitting Nausea and vomiting are not outstanding symptoms each of them mentioned only in 2 cases an important point in differentiation from acute appendicitis A mass in the right lower quadrant of the abdomen was clearly palpable in 3 of the cases

Diarrhea occurred in 14 of the 15 cases constipation is clearly mentioned only once The diarrhea may be and often i transient may last one day and be followed by normal stools and constipation or may last throughout the acute phase of the disease

Hematemesis and tarry stools occurred in one case transient intestinal obstruction once Other unusual manifestations are purpura hemorrhagica (once) erythema nodosum (once) arthralgias (once) these latter unusual signs and symptoms though rare in the acute phase link this abrupt onset with that of the more fully developed clinical picture of chronic ileitis

The radiographic picture an examination which is usually undertaken some days or weeks before the exploratory laparotomy may demonstrate positively the involvement of the terminal ileum In all of the 15 cases subjected to roentgen study the localization and the extent of the lesion could be clearly noted The string sign so characteristic of the fully developed chronic phase of the disease is missing because the cicatrization and the contraction of the lumen of the ileum has not yet had time to develop The mucosal pattern of the terminal loop of ileum is disturbed the lumen narrowed the proximal gut dilated the contour irregular and shaggy The extent of involvement as noted by the radio

TABLE 16

FOLLOW UP OF ACUTE ILEITIS, RECENT SERIES (1957)

	Ca s
\ n ƒ al r —11 case	
Spontaneou resolution	10
Chronic granulomatous pha e	1
Operat ve—4 ca e	
Resection	2
Short-c cu ting ope at on	2
Total	15

Of these 4 operative cases 3 are now well of the 10 cases of spontaneous resolution healing was demon trat d and proved by subsequent negative x ray examination in 3 of the in tances The follow up of the e patients was complete and covered a period of from 2 to 19 years Only one case was complicated by a perirectal absces one by a persistent abdominal wall fistula There were 2 instances of familial involvement in siblings in one instance 2 brothers in another brother and i ter

The favorable progno is a regards acute ileit is borne out by the literature Of 59 cases 33 underwent spontaneou resolution but of 10 operative case 5 died as a re ult of intemperate urgery

Three question arise now (a) Is acute ileitis a di tinct entity or is it a part of the picture of chron c regional ileit ? (b) What i the consensu a to the eventual outcome of cases of acute ileit ? (c) What is the proper urgical or medical treatment of acute ileitis?

DISTINCT ENTITY OR PART OF CHRONIC REGIONAL ILEITIS?

Acute ileitis is undoubtedly an individual phase of regional ileitis It occur mo t frequently as an initial phenomenon capable of complete ub idence in from 25 per cent to approximately 66 per cent of the cases in the remainder advancing to the cla sic picture of chronic gran ulomatou ileit On the other hand in furtherance of the concept of identity of acute and chronic ileit acute ileit may often be regarded as an abrupt exacerbation of the chronic phase of the disea e In many cases a previou hi tory of diarrhea and abdominal pain can be elicited if carefully ou,ht after an occasional bout of temperature a previous rectal operation Out of thi low grade generally unrecognized and unacknowledged course will occur an acute severe episode thi exac erbation will again ub ide and the future course will be identical again with that of chronic regional ileitis (Brown Lehman Eliason and

is associated with constipation and vomiting diarrhea has been noted though exceptionally Endemics of acute gastroenteritis with severe diarrhea may be complicated by a rare incidence of acute suppurative appendicitis (Crohn [8])

Acute mesenteric lymphadenitis simulates both acute ileitis and acute appendicitis and cannot by any clinical symptoms be identified Whether acute mesenteric lymphadenitis and acute ileitis are phases of the same disease process if not identical has been suggested and is still an open question (Jackson) Involvement of the terminal ileum in acute mesenteric lymphadenitis has been mentioned (Strombeck) but the transition of acute lymphadenitis to chronic regional ileitis has not been observed

In this present series the diagnosis was made or confirmed by laparotomy in 9 of the 15 cases or was substantiated at a subsequent operation

The prognosis in acute ileitis is good in the former series of 16 cases one died due to a brash surgeon's undertaking resection of the lesion in the presence of a fulminating disease In this present or latter series there were no deaths

The follow up of the earlier series terminating in 1949 was tabulated as follows

TABLE 15

FOLLOW UP OF ACUTE ILEITIS (1949)

	Cases
Nonoperative—4 cases	
Spontaneous resolution	2
Chronic granulomatous phase	1
No follow up	1
Operative—12 cases	
Resection—death	1
Spontaneous resolution—well	2
Chronic granulomatous phase	4
Subsequent short circuiting operation	4
Subsequent resection	1
Total	16

Thus it will be noted that only 4 cases of the 16 or 25 per cent went on to spontaneous resolution the remaining cases lapsing into the chronic granulomatous phase of the disease

The present more recent series demonstrates the subsequent course as seen in the follow up

TABLE 16

FOLLOW-UP OF ACUTE ILEITIS RECENT SERIES (1957)

	Cases
Nonoperative—11 cases	
Spontaneous resolution	10
Chronic granulomatous phase	1
Operative—4 cases	
Resection	2
Short-circuiting operation	2
Total	15

Of these 4 operative cases 3 are now well; of the 10 cases of spontaneous resolution healing was demonstrated and proved by subsequent negative x-ray examinations in 3 of the instances. The follow-up of these patients was complete and covered a period of from 2 to 19 years. Only one case was complicated by a perirectal abscess, one by a persistent abdominal wall fistula. There were 2 instances of familial involvement in siblings; in one instance 2 brothers, in another brother and sister.

The favorable prognosis as regards acute ileitis is borne out by the literature. Of 59 cases, 33 underwent spontaneous resolution, but of 10 operative cases 5 died as a result of intemperate surgery.

Three questions arise now: (a) Is acute ileitis a distinct entity or is it a part of the picture of chronic regional ileitis? (b) What is the consensus as to the eventual outcome of cases of acute ileitis? (c) What is the proper surgical or medical treatment of acute ileitis?

Distinct Entity or Part of Chronic Regional Ileitis?

Acute ileitis is undoubtedly an individual phase of regional ileitis. It occurs most frequently as an initial phenomenon capable of complete subsidence in from 25 per cent to approximately 66 per cent of the cases, in the remainder advancing to the classic picture of chronic granulomatous ileitis. On the other hand, in furtherance of the concept of identity of acute and chronic ileitis, acute ileitis may often be regarded as an abrupt exacerbation of the chronic phase of the disease. In many cases a previous history of diarrhea and abdominal pain can be elicited if carefully sought after, an occasional bout of temperature, a previous rectal operation. Out of this low-grade, generally unrecognized and unacknowledged course will occur an acute severe episode; this exacerbation will again subside and the future course will be identical again with that of chronic regional ileitis (Brown, Lehman, Elsason and

Johnson Smithy) Lyall even expresses the view that chronic regional ileitis represents only the end stages of acute ileitis with subsequent fibrosis and cicatrization The process is primarily an acute one which tends to subside so that the appearance thought by some to indicate a chronic inflammation are really attempts at repair

Eventual Outcome

In our own two combined series (1949 and 1957) 14 out of 31 ca es of acute ileitis showed complete resolution as judged by subsidence of all symptoms and in many cases by the change of a positive x ray picture to that of a negative roentgenogram within the course of a few months to a year The follow up of 2 to 19 years is an assurance that this healing is a positive one since most of these cases have been fol lowed 8 to 19 years without showing signs of a recurrence If acute ileitis were merely a phase of chronic regional ileitis then the percent age of recurrence in later years should be much higher even though it is difficult to think of a granulomatous di ease originating in an acute process

Meyer and Ro t noted spontaneou resolution in 3 out of 4 cases of acute ileitis They controlled their observations by radiographic studies in one case involving a child of 7 years of age seven weeks after the exploratory operation the involved ileum appeared roentgen ographically negative and free of disease Another case in an adult female was well one month after the operation radiographic examination re vealed a normal terminal ileum An adult Negro male was ob erved for 1½ years after exploratory operation for acute ileitis and was and remained radiographically negative for any residual signs of the previou inflammatory focu in the terminal ileum

In the series of Brown and Donald 7 out of 10 of the acute ca es were well 6 of them three or more years after the simple exploratory operation The series of Warren and Sommers included 15 cases of acceptable acute ileiti 12 of the e or 80 per cent regressed 2 pro gressed and one died McKinnon reported the spontaneou cure in a case of acute regional ileitis 2½ years after the exploratory operation the patient wa well and the radiographic examination which previously had hown involvement of the terminal ileum was now entirely negative

The sub idence and complete cure of acute ileiti is convincingly shown by most of the ca es in the reported literature thus Meyers and Rosi in a follow up of 1 month 7 weeks and 1½ years Brown 2 years

3 years and 4 years Bisgard and Hencke 2 years Rixford in discussing a paper by Mixter cites a case which had remained well for 8 years after an exploratory operation In the series reported by Eliason and Johnson 4 cases have remained well for 2 to 6 years 4 additional cases have remained well for not less than 1 year One case by Smithy was well 6 years after exploration the second case showed some radiographic evidence of the dise e 6 weeks after exploratory operation but was well with a negative x ray examination 15 months later In Lehman s series of 7 ca es 4 have been free of symptom of the disease from 14 months to 9½ years after the exploratory operation Kross followed his one case for 7 years of complete restitution Pugh reports 2 cases of acute ileitis with spontaneous recovery One case was operated on and acute terminal ileitis observed 6 months later the case was reoperated on and scarcely any evidence of the original lesion was found In the second case after an operation for acute ileiti the patient wa followed by repeated x ray examination until a completely normal bowel was observed roentgenographically Probstein and Gruenfeld described acute ileitis of terminal ileum with severe hemorrhage enterostomy Three months later at closing of the fistula the process appeared healed A small section of the previou ly involved ileum was removed for biop y the micro copic sections revealed only slight round cell infiltration of the subserosa In a second case only an enterostomy was performed for severe terminal ileitis (15 cm) Two years later the patient was entirely well

Medical or Surgical Treatment

The con ervative treatment of acute ileitis consists of avoiding exploratory laparotomy where the best judgment of the ob ervers in terni t and surgeon warrants such a course and in the administration of antibiotics sulfathalidin or better the broad spectrum antibiotics such as achromycin erythromycin or streptomycin in large doses usually orally

The urgical therapy at the time of the exploratory operation re olve itself into three possible courses of action

(1) Simple closure of the abdomen (2) appendectomy alone clo ure of abdomen without drainage (3) a radical procedure (resection or h rt-circuiting)

When the preoperative diagnosis can be made with any sense of as urance uch as in the presence of diarrhea or a pos ible previous

Johnson Smithy) Lyall even expresses the view that chronic regional ileitis represents only the end stages of acute ileitis with subsequent fibrosis and cicatrization The process is primarily an acute one which tends to subside so that the appearance thought by some to indicate a chronic inflammation are really attempts at repair

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Chapter 16 Ileo-Jejunitis

ILEO-JEJUNITIS may be defined as that form or type of chronic enteritis in which the granulomatous process typical of that disease involves the jejunum either as an extension from the ileum or as an independent lesion limited to all or some of the upper segments of the small bowel

Very soon after the original publication in 1932 of regional or terminal ileitis it was recognized by Harris Bell and Brunn that the upper ileum and the jejunum could be and were also involved in an almost identical pathologic process The literature year by year has added new case histories most of them on the regional form of jejunitis As early as 1934 Brown Bargen and Weber reported 3 cases of enteritis with the lesion restricted to the jejunum In 1936 Meyer and Rosi mentioned a case with the inflammatory process localized in the jejunum In 1937 Pemberton and Brown already noted that 3 of 37 cases of regional enteritis were entirely restricted to localized segments of the jejunum Lakely and Lisa reported in detail 2 cases of high jejunitis resected ending fatally and carefully studied at autopsy These were both localized lesions high in the jejunum causing clinical intestinal obstruction Ravdin and Johnston in 1939 cited 16 cases of sole involvement of the jejunum in cases culled from the literature

In 1941 Crohn and Yunich published an analysis of 17 cases of diffuse ileo-jejunitis with a clinical analysis of the outstanding symptom and the therapeutic approach to the problem The differentiation of ileo-jejunitis from sprue was particularly emphasized Sussman and Wachtel added the distinguishing roentgenographic features in an analysis of 23 cases of granulomatous jejuno-ileitis

Jejunitis or ileo-jejunitis is not a separate or different disease in all of its major characteristics it is but a subtype of the more common form of regional ileitis. In its pathology as a granulomatous lesion it is in no major way different from ileitis except in its anatomic distribution one notes the same clinical characteristics fever diarrhea a mass by palpation fistulas rectal complication and anemia But the degrees of involvement are different the pathologic process is spread over a wider area the local intensity is less marked in any one segment and fistulas

history of diarrhea fever or a rectal fistula no exploration is justified In the absence of vomiting or rebound tenderness or of a mass with low fever and a low leukocyte count exploratory operation should be avoided If operation is undertaken under a false diagnosis simple clo ure of the abdomen without drainage is advocated

If however the abdomen is opened and the exploration reveals an acute ileitis should the appendix be removed? There seems little justi fication for such procedure Though the practice of appendectomy i common under such circumstances the pathologic report if scrutinized is invariably either negative or else one of chronic inflammation On the other hand there is really no good evidence to show that appendec tomy performed at thi time is more prone or conducive to abdominal wall fistula In the total group of 31 cases appendectomy was performed in most of them yet only 2 abdominal wall fistulas are noted a rather low incidence Since acute gangrenous appendicitis does occur not in frequently in chronic regional ileitis removal can be advocated as a prophylactic measure

Is a radical procedure such a resection or a short circuiting opera tion ever indicated at the time of exploration? The earlier surgeons with experience in this field often advocated radical re ection at the time of exploration The mortality was high however even forbidding

Since the establishment of the fact that spontaneou healing wa not only possible but likely in a large percentage of cases of acute ileiti the consensus favors expectant waiting and noninterference (Koster et al Brown Mailer Eliason and Johnson Smithy Waugh Meyer and Rosi)

That resection or a short circuiting procedure may eventually be come necessary is evident in the follow up of our cases of acute ileitis In our combined eries (1949 and 1957) of 31 cases 9 were sub e quently subjected to operation (resection 3 short circuiting 6) most of them with permanent good result although the number of ca e is too small to permit tabulated re ult

2. Involvement of the terminal ileum and upper jejunum by skip lesion—3 cases
3. The pathologic process involving upper ileum and lower jejunum continuously—10 cases
4. Diffuse ileo jejunitis—40 cases
5. *Diffuse jejunitis with extension upward to involve duodenum*—4 cases and stomach—2 cases
6. *Localized jejunitis* chronic or acute—9 cases

Involvement of the Jejunum by Upward Extension from a Chronologically Older Process in the Ileum—2 Cases

Regional ileitis almost always remains in the distal ileum as such and even over the course of years rarely extends upward. However a rare form exists of mucosal or better expressed submucosal ileitis in which the pathologic process advances in an oral direction, frequently at a rapid pace to invade the jejunum. We have observed only two instances of this submucosal spread into the jejunum (figs 23 26)

Jejunitis as a complication of ileitis is also seen after unsuccessful surgical procedures in which repeated recurrences take place. Following a resection or a short circuiting of the initial terminal ileitis a recurrence takes place in the new terminal segment of ileum. Another resection is carried out followed by a new recurrence. A third resection may occasionally be attempted; any further recurrences may now carry the process up into the jejunum, for the sacrifice of involved recurrent ileum may necessitate the resection of a wider area until the whole ileum has been dispensed with and the jejunum is invaded by the malignant extension of the disease process.

Involvement of the Terminal Ileum and of the Upper Jejunum as a Massive Skip Lesion—3 Cases

Here one sees an exaggerated skipped area in which the original site of the disease resides in the terminal ileum and by an enormous jump establishes a *skip lesion high in the jejunum*. These are fortunately rare episodes occurring only in 3 cases in the series but posing a difficult question both in pathology and in therapy. It is most difficult to understand by any view of the pathology of the disease how an extension from an original focus in the terminal ileum can exclude the entire remaining length of the small bowel and reimplant itself in the

and rectal complications are fewer But the general constitutional disturbance is greater nutritional absorption is markedly impaired fever the enlarged spleen the clubbing of the fingers indicate the degree of absorption of the toxic products of the disease skeletal growth is impaired Hypoproteinemia is a characteristic of the advanced pathologic state

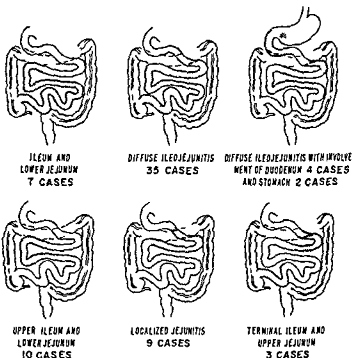


Fig 61 Anatomical distribution of ileo jejunitis

The course is low grade often less severe a considerable degree of spontaneous healing is possible The disease is less amenable to surgical therapy than terminal or regional ileitis

Ileo jejunitis should be considered and studied in its various forms in its anatomic and pathologic variation as illustrated in the 70 cases of ileo jejunitis which constitute the present series (fig 61)

1 As an extension upward of an etiologic older process in the ileum—2 case

Fistulas rarely form the process is typically granulomatous with marked thickening and cobble tone linear erosions of the submucosa and mucosa longitudinally and transversely Attempts at local excision require massive surgical resection with great risk of life and little assurance of permanent cure Moreover these localized forms are relatively benign and require only conservative forms of therapy

Diffuse Ileo-Jejunitis—40 Cases

This is the mo t common form seen and constitutes a group of 40 of the total 70 cases under study *Here the whole ileum and the whole or most of the jejunum are involved in a continuous process* Occasion

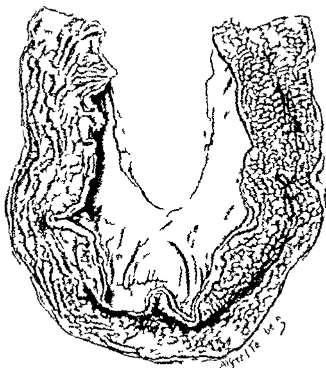


Fig 63 Path l gi in l em nt of uppe ileum and jej num

upper jejunum Certainly not by continuity probably not by lymphatic extension Can one contemplate the hypothesis suggested in the German literature[315] that originally all of the bowel had been infected and that the disease resolved itself everywhere except at those extremities of the small intestine? Peculiarly these cases lend themselves to surgical therapy namely a local excision of the upper skip lesion in the jejunum and a short circuiting of the distal lesion in the ileum

The Pathologic Process Involving Upper Ileum and Lower Jejunum as a Continuous Process—10 Cases

This is a not uncommon type of the disease observation of a long period has demonstrated that the process further extends neither upward nor distally but remains static over the course of the years



Fig 67 Lower jejunum upper ileum involved Onset with gross hemorrhage melaena diarrhea and continuous fever

jejunum and the whole ileum being the seat of one continuous process of disease

Chronologically it is impossible to determine which segment is the primary seat of the disease In practically all of this group the disease had universally involved the whole of the small bowel when first recognized so that it was impossible to state whether the initial process was in the upper jejunum or in the lower ileum Presumably in this severer type the whole small bowel is simultaneously involved

Barbour and Stokes in 1936 described a case which at autopsy was shown to have 13 areas of alternate thickening and thinning of the entire small intestine from pylorus to the ileo cecal valve Halloway s Case 5 showed definite involvement of the third part of the duodenum as well as the terminal ileum and intermediate segments Rees has described the case of a 30 year old Negress who at operation presented the picture of multiple intestinal obstructions at three points in the upper jejunum due to segmental jejunitis resection en masse was surgically successful

Diffuse Jejunitis with Extension Upward to Involve Duodenum—4 Cases and Stomach—2 Cases

These cases occurred all in adults In all of these six cases the process occupied anatomically the upper jejunum with extension into the 4th 3rd and even 2nd portions of the duodenum and in two case with isolated lesions in the antrum of the stomach the ileum was not incriminated in any of these six cases

Localized Jejunitis Chronic or Acute—9 Cases

The acute case have been described in the literature one of our cases was acute well defined at exploratory laparotomy this case went on to spontaneous resolution The other 5 cases were chronic with localized involvement of a segment of the jejunum clearly demarcated by x ray and restricted to from a few inches (6—8) to 1 to 2 feet of disease Fistulas and perforation have not been encountered This type again represents a relatively benign example of the disease

In 3 of the cases isolated areas of jejunum solely were the seat of the disease one was 4 inches one 2 feet and one 4 feet from the fossa of Treitz a small isolated segment of jejunum 6 to 8 inches in length being the seat of the pathologic process

Instances of isolated jejunitis have been published by Johnson by

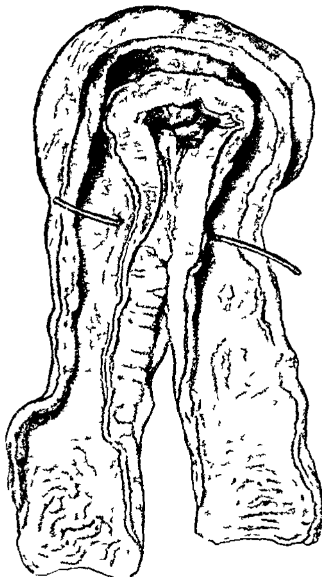


Fig 64 Pathologic lesion involving lower jejunum fistula between loops of small intestine

ally in the uppermost jejunum the process is interrupted by the appearance of skip lesions separated by areas of normal mucosa the lower

and Wright as seen at autopsy in 2 cases at Bellevue Hospital The more recent German literature describes isolated case and cases seemingly occurring a an endemic of extremely grave severity Wigand noted 37 cases of necrotic jejuniti of which 27 died the average age of the patients was 55 years the symptom were acute often fulminating and characterized by high fever and inten e pro tration Fick and Wolken described (in 1949) 18 cases of necrotic jejunitis from Hamburg Germany 16 of the 18 cases died within 7 days 2 were reportedly saved by early resection The onset wa acute with unusually severe and violent abdominal pain nausea and vomiting and circulatory collapse If the patient survives the proces resolve itself into the u ual form of chronic enteritis

The whole subject of jejunitis acuta has been summarized in the Acta Chirurgica Scandinavica by Johan Hertzberg in 1954 During the last war a large number of cases of the disease were reported in Norway and in Germany Hausen and his collaborator mention 364 cases of enteritis necroticans in Lubeck in 1946-1947

Whether acute phlegmonous or n crotic jejuniti i in any way related to isolated localized jejunitis as we set it is questionable Our cases of acute ileitis or acute jejunitis do not die many of them if they do not resolve immediately lap e into the chronic granulomatous form of the disease whether in ileum or jejunum It may well be that the European type of acute necrotic jejunitis is entirely unrelated

Eti logy

In this series of 70 cases 28 were female and 47 were males indicating a preponderance of male involvement of almost 2 to 1 It is possible that the series i too small to warrant a scientifically ac urate conclusion but throughout the series the major involvement of males is a striking characteristic. (In regional ileitis the proportion of males to females is 5 to 4) Sussman and Wachtel found a similar incidence of 3 males to 1 female in ileo jejunitis

The main brunt of the disea e seem to fall in the second decade of life the third and the fourth decades together contributing an almost equal number After the age of 40 only a rare exceptional case is seen The extreme youth of mo t of these cases of ileo-jejunitis i a striking fact In the series of 23 case of granulomatous jejuno-ileitis publi hed by Sussman and Wachtel the average age incidence was 27 0 years the range varying from 9 years to 65 years of age

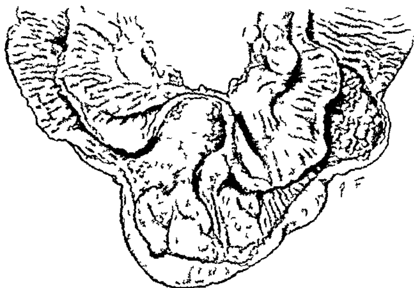


FIG 65 Localized jejunitis occupying uppermost area of jejunum Alternate constriction and dilatation mesenteric lymph n des Characteristic cobblestone appearance identical with that seen in the terminal form of ileitis

Brewster by Gendel and Beaver by Koenig and by Lyons and Garlock James published 3 cases of regional jejunitis of unusual interest In one case the whole jejunum from duodenum to ileum was involved An anastomosis was made between the stomach and the upper ileum in order to short circuit the lesion In a second case the terminal duodenum and 18 inches of proximal jejunum showed thickened and beefy walls here gastro jejunostomy wa performed In the third case 2½ feet of the proximal jejunum showed on exploration chronic inflammatory change again gastro-jejuno tomy was performed Ca es of primary regional enteritis involving the jejunum following trauma were reported by Browne and McHardy and by Spellberg and Gray

Kazmann and Barnett in 1951 published a case of acute localized upper jejuniti the diagnosis confirmed at exploratory laparotomy No resection was attempted the patient made a rapid recovery from the surgical procedure and remained asymptomatic for two sub equent years of ob ervation

An acute phlegmonou or necrotizing type wa described by Clark

thickening edema and congestion Since much healing i capable in the upper small bowel areas of contraction moderate or extreme may appear with intervening dilated and distended loop of intermediate bowel (fig 65) Where two or more areas of constriction occur the intermediate bowel may be much distended This over distended loop may give ri e to necrosis of the bowel wall with abce s formation Or a perijejunal abscess may form in the thickened and inflamed mesentery the absce s being walled off and localized When such an ab cess forms it may become adheren to the abdominal wall at the site of the scar of a previous incision and d scharge its conten Fecal fis ulas to the abdomi nal wall are however rare The lymph node of the me entery are enlarged and succulent similar to tho e seen in distal terminal ileitis Micro copically the process is identical to that of ileitis and of intestinal granulomata in general Miliary like tubercles consisting of lymphoid and epithelioid mononuclear and plasma cells are common and frequently en lose giant cells pre umably of foreign body nature The lymphoid follicles are hyperpla tic with active germinal centers In their excellent article Sussman and Wachtel describe the pathology as well as the radio logic appearance of the disease a occurring in three stages namely acute subacute and chronic The acute stage i characterized by edema and thickening of the mucosa and of the adjoined mesentery the subacute stage by a granular and hypertrophic mucosa containing punched out ulcera tions with smooth or irregular edge th ulcer being either longitudinal or transverse to the axis of the bowel early polypoid proliferation and evident kip le ions are discernible The chron s age is characterized by thickening and fibrosis alternating areas of atrophic and hypertrophic mu osa multiple areas of stenosi the ero a b ing covered by a shaggy exudate This d scription in ludes the findings at four autopsies and the inte tinal biopsies obtained at three of eight exploratory laparotomies and represents an accurate and painstaking study of the pathologic change in the three variou pha es of the dis ase

Several forms of i olated jejunal ulcers appear in the literature although there i some question as to the identity of such ulcer with the granulomatous forms which are recognized as ileo jejunitis Richard son in 1922 wa re ponsible for the first American description he cited 2 ca es of jejunal ulcer with stricture and perforation Buckstein gave a good de cription of primary ulcer of the jejunum Robin on and Wise in 1940 reviewed the whole literature and culled the large number of

The age incidence in this series is striking and indicates a preponderance of involvement in the earlier decades of life (table 17)

TABLE 17

ILEO JEJUNITIS AGE INCIDENCE

Age at onset in Years	*No of Cases*
1 10	5
10 20	27
20 30	23
30 40	11
40 50	3
50 60	0
60 70	1
Total	70 cases

No new or significant factors as to the causation of ileo jejunitis are known as distinct from regional ileitis The same fundamental ignorance as to causation and etiology which covers ileitis applies also negatively to ileo jejunitis In only one of the 70 cases in the group which forms the basis of this study was physical trauma attributed as a causative factor Trauma however has exceptionally been recited in the literature (Browne and McHardy Spellberg and Gray)

Pathology

The pathology of ileo jejunitis differs little from that of regional ileitis Grossly the small intestine is bluish red in appearance the serosa streaked by inflamed lymphatics The wall is thickened coarse and firm where long standing healing has taken place the lumen may be contracted and the wall of the gut puckered When the resected specimen is opened the mucosa is cobble toned in appearance as seen in ileitis cross hatching of longitudinal and transverse ulcerations creating that appearance The mucosa is thrown up and prominent in places appearing as and even assuming a polypoid excrescent form True inflammatory polyps occur frequently and can be visualized in the roentgenogram The ulcers in the mucosa penetrate to the inflamed thickened submucosa these ulcers rarely penetrate more deeply and do not with rare exception form fistulous tract The whole wall submucosa muscularis and serosa is involved in the granulomatous and cicatricial process as evidenced by

Diarrhea is the most constant symptom occurring in most of the 70 cases in this series constipation is noted 4 times only normal bowel movements prevailing in the remaining instances The diarrhea is never extreme averaging usually 2 to 4 movements per 24 hours The stools are mushy or semisolid mixed with thin mucus occasionally they are watery Pus is never seen gross blood in flecks only exceptionally The guaiac reaction wa positive in 10 cases negative in the remainder In fact it is not unu ual to have negative guaiac reaction in the fece of proved ca es throughout the course of the disease

Abdominal pain is another almost constant symptom having occurred in 56 of the 70 cases in this group The abdominal pains are crampy in nature diffused over the abdomen or more likely to be localized over the left upper quadrant The pain may be mild and a sociated with the desire to defecate or severe and definitely predefactory in timing With the passage of fluid feces and ga accompanied by an audible gurgling the cramp is allayed When ob tructive phenomena are present the abdominal cramps are more or most severe occasionally accompanied by vomiting

Gross hemorrhage occurred once in this present serie In a previously studied eries it occurred three times as an initial symptom out of 17 ob erved cases The gross hemorrhage takes the form of melaena (5 cases) though once it was accompanied by a brisk hematemesis The hemorrhage while profuse is never exsanguinating and u ually not as o ciated with shock

Symptoms of obstruction are frequent and occurred in 17 of the 70 cases The intestinal obstruction is frequently of low grade relieved by the Harri tube few of the ca es being of such severity as to require operation for advanced obstructive phenomena The obstruction is usually inflammatory in nature and is due to edema of the bowel wall possibly accompanied by a perijejunal or a mesenteric ab cess and subsiding as the inflammatory process recedes Vomiting was noted in 5 cases Browne and McHardy mention obstruction as one of the symptoms in their ca e of a Negro boy who developed a localized jejunitis following a severe abdominal trauma

Anorexia and weight loss are common manife tations The loss of appetite is spotty and occurs during acute exacerbation of the chronic process at other times appetite may be well maintained

The weight loss may be very severe amounting in some of our

36 cases of solitary ulcers of the small bowel of which 7 were jejunal Dowdle adds a case of multiple primary nonspecific jejunal ulcers with duodenal dilatation the bowel was obstructed not much below the ligament of Treitz with dilatation and thickening of the intestine above the strictured area

Symptomatology

The rare acute forms of ileo jejunitis are characterized by abrupt onset with fever diarrhea and abdominal pain a mass may be palpable in the left upper abdomen a high leukocyte count is common Clark and Wright cite 12 cases from the literature in which the duodenum was involved associated with vomiting

Husebye presented 14 cases of acute phlegmonous jejunitis as seen by x ray in six instances the diagnosis rested essentially on the roentgen appearance of the films seven of the fourteen patients recovered The roentgen findings were characteristic and consisted of (1) reduced diaphragmatic movements on one or both sides (2) scout films which revealed distended loops of gut over the left abdomen (3) erect films which revealed fluid level (4) barium meal procedure which showed the mucosal relief to be roughly jagged with irregular circular folds partly sharp and partly blunt

The classic form of chronic ileo jejunitis or jejunitis is that of a low grade granulomatous inflammatory lesion involving primarily the jejunum either continuous with a similar process in the ileum or else associated with an independent lesion in the distal ileum

The onset is usually gradual and prolonged lasting from six month to fourteen years or more The actual onset i often difficult to estimate since the occasional slight diarrhea mild fever or loss of weight i little noticeable

The outstanding clinical symptoms are (a) low grade fever (b) diarrhea (c) severe abdominal pain (d) gro hemorrhage (e) symptoms of obstruction (f) anorexia (g) lo s of weight (h) anemia

Fever was pre ent in 16 of the 70 cases in this eries the fever i intermittent in type higher in the later afternoon or evening it may rise to 103 F though usually the range is between 100 and 102 F temperature chills are occasionally noted The fever may be so mild a to be almost imperceptible and may not be accompanied by malai e or pro tration The fever may be paroxysmal remaining continuously for several weeks or months or may be interrupted by periods of apyrexia

narrowing with localized dilatation and constricting Serum calcium was 8 0 and 8 2 milligrams per cent inorganic phosphorus 3 5 and 3 8 milligrams Vitamin A absorption of 250 000 USP units was only slightly below normal levels fasting serum carotene almost normal The patient improved rapidly under high protein diet and amino acid concentrates The intravenous administration of amino acids did not improve the nitrogen balance or create nitrogen retention in the metabolism studies

Loss of fat soluble vitamins was especially emphasized in Albright and Stewart s report The case a woman aged 35 years had undergone 4 successive operations for ileitis and recurrent ileitis including 2 extensive intestinal resections Protracted severe abdominal cramp and diarrhea resulted in tetany and a state of marked vitamin deficiency The prothrombin time was found to be only 13 per cent of normal indicating a marked associated vitamin K deficiency Vitamin C was within normal range Fat soluble vitamin A was somewhat deficient 8 2 units per 100 cc of serum (normal 10 20 unit) carotenoids somewhat diminished and associated with an xeroderma of the breast and abdomen Fat soluble steroids particularly the quantity of 17 keto teroids in the urine were practically absent The tetany responded rapidly to large doses of vitamin D 500 000 USP units daily The results of treatment in the form of liberal do age with all of the fat soluble vitamin preparations were clinically dramatic

An unu ually exaggerated degree of hypoproteinemia was noted in a diffu e case of ileo jejunitis by Casten At a previous operation an anastomosi between the upper jejunum and the tranverse colon had been performed because of a diffuse inflammatory process involving all of the ileum and the lower jejunum Extreme malnutrition and evidences of hypoproteinemia were soon evident The total serum proteins fell to 3 1 grams per 100 cc the albumin fraction being 1 1 Gm and the globulin 2 Gm (albumin globulin ratio 0 55) Most observers conclude that the critical level of serum protein being 5 0 Gm per 100 cc edema will invariably result when the blood level falls below that point Hypoproteinemia occurs 5 times in this series

Bl o d Changes The white cell count varies only a little from the normal a very mild leukocytosis up to 8 000 to 10 000 or even 18 000 white blood cells may be noted though most usually the count i within the lower range of normal Eosinophilia as seen in ulcerative colitis i unusual although it wa seen in 5 patients of our previous series up to 14 per cent of eosinophiles being present in the blood smears A mild

cases to as much as 50 pounds in a stout girl The average loss of weight in our previous series was 17½ pounds During the healing phases with remissions of the fever and diarrhea the weight may be rapidly regained 15 25 or even 50 pounds may be added during prolonged remissions of the symptoms

The *nutrition* is usually poor skin is dry mucous membranes pallid An extreme degree of malnutrition with inanition and loss of strength marks the end stages of lethal cases Retarded growth and retarded sex maturation are commonly observed in those young adolescents who are so frequently affected by the disease at a prepubertal age With the recovery from the severe phase and with healing of the lesion advancing weight growth in height and secondary sex maturation may replace the hypogonadalism seen in the adolescent years One of our earlier cases who had remained stunted in growth and devoid of secondary sex characteristics later recovered fully from the diffuse ileo jejunitis from which he had suffered grew to be a strong well developed man married and was the father of two children

The menses are rarely skipped in ileitis as they are in severe ulcerative colitis Several cases of ileo jejunitis have married and borne normal children without detriment to their general health or difficulty and without the induction of a recurrence of the disease process

Aphthous stomatitis (3 cases) furunculosis erythema nodosum epidermolysis bullosa were each seen once Phlyctenular conjunctivitis was twice seen occasionally one notes bleeding gums glossitis as evidence of nicotinamide deficiency and riboflavin deficiency as marked by cheilosis though these are extremely rare Vitamin A deficiencies night blindness and the bone changes of vitamin D deficiency have not been noted

Killian and Ingelfinger studied the nutritional problems presented by a patient with extensive ileo jejunitis A 23 year old boy with a previous history of a loss of 40 pounds of weight was aboard a ship torpedoed during the recent war and was exposed in a life raft for eight days He was found in a state of extreme malnutrition emaciated dehydrated with pitting edema of the lower extremities The tongue was smooth fever up to 102 F hemoglobin 54 per cent red blood cell 1 200 000 hematocrit 22 per cent Serum protein was markedly reduced to 4 85 grams per 100 cc albumin 2 34 globulin 2 51 grams per cent Clubbing of the fingers was present the glucose tolerance test showed hypoglycemia with a low tolerance curve By x ray examination the lower jejunum and the ileum showed marked irregularities and points of

in a very severe case of ileo jejunitis The albumin globulin ratio is disturbed approaching a ratio of one but rarely completely reversed

The urea phosphorous blood chlorides and blood sugar are but slightly if at all lowered The blood calcium may be materially reduced 2 of the patients in our present series having shown frank symptoms of tetany

Gastric analysis showed normal titrable acidity in all cases except one of achylia gastrica

The physical examination of a case of ileo jejunitis may not be



Fig 66 Clubbing of finger in a of diffuse ileo jejunitis with involvement of the whole jejunum and the upper ileum palpable spleen

secondary anemia was present in 12 out of the 36 cases in this series the range being usually between 72 and 50 per cent hemoglobin (Sahli) A macrocytic hyperchromic type of anemia occurred once in our previous series with a color index of 1 3 In this eries of 36 cases hyperchromic anemia was not observed even though the anemia was at times severe and the intestinal absorption severely compromised as evidenced by *hypoproteinemia* *The hyperchromic anemia in ileo jejunitis is usually* not beneficially influenced by intramuscular injections of crude liver extract the reticulocyte response attaining a level of only 7 per cent this in contrast to its more successful therapeutic result in cases of non tropical sprue

The occurrence of macrocytic anemia in association with intestinal lesions particularly intestinal strictures and anastomoses was amply demonstrated in the literature by Faber Hale White Meulengracht and by Hurst Butt and Watkins mention 7 cases of diffuse ileitis with macrocytic anemia in 6 of which a fecal fistula coexisted With proper reconstructive surgical intervention the macrocytic type of anemia could be returned to a normal blood picture They rightly ascribe the hyper chromic anemia to the abnormal interference with absorption and im proper utilization of the effective hemopoietic fraction of the diet Plum and Warburg in a publication entitled Hematological changes e pecially megalocytic anemia in regional ileitis describe 4 cases under their personal observation in which the blood picture was typical of that of a hyperchromic anemia The hemoglobin values ranged as low as 20 per cent red blood cell count as low as 1 410 000 cells color *index 1 12 1 19 1 15 1 05 at the point of greatest severity In one* case the jejunum seemed definitely to be involved Barker and Hummel similarly quote a case of ileitis with resection and a secondary short circuiting operation and a con equent hyperchromic anemia

Sprue a disease without noticeable organic changes in the intestinal mucosa but with completely deficient intestinal absorption is often characterized by a hyperchromic or macrocytic type of anemia Ileo-jejunitis by contrast is a disease with extensive organic destruction of wide areas of *intestinal mucosa yet ab orption is better maintained in* spite of severe and exten ive ulceration A hyperchromic type of anemia is rare

The erythrocytic edimentation rate may be somewhat accelerated as seen in 5 patient The total blood protein of the plasma i appreciably diminished in the more severe cases (5 8 Gm) reaching a minimum of 4 0 4 4 and 4 5 grams per 100 cc in 3 cases and as low as 3 8 grams

striction and dilatation which are present as obstructive phenomena in ileo-jejunitis are absent in sprue (figs 67 and 68)



Fig 67 Ileo-jejunitis involving upper ileum and lower jejunum Resection in continuity at the Mayo Clinic complete restoration to health

In ileo-jejunitis marked general clinical improvement may be noted as a result of general hygienic measures and the forceful administration of the steroids but the diffuse string signs throughout the ileum and jejunum are irreversible and remain permanent even though general good health and nutrition have been restored In cases of diffuse ileo-jejunitis without obstruction observed over a course of years (10 22 years) complete subsidence of symptoms with regain of 50 pounds or

noteworthy Some of the cases show well maintained nutrition others may give evidence of pallor and extreme malnutrition in the later stages of a deteriorating status A mass is occasionally pre ent (8 cases) usually in the left upper abdomen corresponding to the inflamed mesentery of the jejunum with the associated granulomatous loops of bowel Such a mass may often be adherent to the anterior abdominal wall forming a localized abscess that requires incision and drainage External fistula to the abdominal wall occurred 7 times in thi series Internal fistulas ileum to jejunum or jejunum to jejunum occurred 4 times

In case of localized subacute intestinal obstruction the whole abdomen may be distended visible peristalsis was seen when the degree of obstruction became complete and almost always associated with vomiting The edge of the spleen was distinctly felt 5 times in this series frequently associated with clubbing of the fingers which was noted 13 times in all

The clubbing of the fingers and occasionally also of the toes is a significant observation and indicates the extreme degree of constitutional alteration invoked by so diffuse an intestinal dysfunction (fig 66) Cooke found clubbing of the fingers to be present in 48 out of 90 cases[8]

Rectal complications do not occur with the same frequency as in regional ileitis In this series peri rectal abscesses and fistulas occurred 11 times a vesical fistula was never observed

Differential Diagnosis

The main point of interest lie in differentiating high ileo jejuniti from sprue and from the secondary vitamin deficiency manifestations Sprue is characterized by typical frothy and fatty stools by a severe secondary anemia or by one of hyperchromic type with a high color index Fever is ab ent the stool do not contain blood gross hemorrhage either as melaena or hematemesi is missing The sprue ca e or that of vitamin deficiency reacts well to deep injections of crude liver extract vitamin B complex and of B but particularly now is well controlled by steroid therapy especially hydrocortone in large do es by oral administration or parenterally With such therapy the sprue or deficiency case may show a partial or complete reversal of the disturbed muco al pattern in the mall bowel with a restitution to the normal appearance

The lower or terminal ileum i usually free of di ease in sprue in jejuniti and certainly in ileo-jejunitis the distal ileum constitutes a major area of pathologic di turbance The intermittent areas of con



Fig 69 D ffu e ileo jej n ti ob d over a cour e of everal yea

uch a ac ompany evere ulcerative colitis give roentgenographic changes imilar to tho e of sprue and often to those of mild d ffu e jejuniti They have been de ribed by Snell and Camp by Mackie and Pound and by Adler berg and Weingarten Mild puddling delay in jejunal loops irregular utline of the upper ileum and lo ver jejunum such as occur in pr ie and in jejuniti may be present there are no manifestations of delayed m tility and no obstructive or polypoid change in the roentgeno grams



Fig 68 Diffu e le j junit n a boy of 17 years of age confirmed by exploratory operat n Rap d dow h ll cour e

more in weight has been repeatedly ob erved the continual radiographic examinations year after year how the same intermittent string sign occupying ileum and jejunum a een at the fir t ob ervation Evidently permanent scarring and cicatrization of the inte tinal wall had persi ted in spite of restoration of health and integrum

The vitamin deficiency tates with disturbance of fat metaboli m

ileitis must be recognized in the differential diagnosis where more common diseases of febrile nature receive first presumptive consideration. Diseases characterized by continuous fever with low leukocyte counts include such syndromes as brucellosis, rheumatic fever, periarteritis nodosa and lupus erythematosus disseminatus. The advent of diarrhea so often overlooked or ignored indicates the possibility if not the likelihood of ileo jejunitis being the true cause of the febrile state (fig 70)



FIG 71 Sprue—characteristic segmentation in loops of small bowel

Whipple's Disease

Avery Jones and Paulley called attention to the possible relationship of intestinal granulomatous lipodystrophy and regional ileitis. Intestinal lipodystrophy may simulate ileo jejunitis and requires differentiation from it. This condition is characterized by a sprue like diarrhea



FIG 70 Same case as figure 66 two and a half years later subsidence of symptoms gain of fifty pounds of weight Absence of stenosis and stricturing

Hodgkin s disease of the small bowel and diffuse multicentric sarcomatosis of the mesenteric lymph nodes with intestinal involvement are rare diseases which simulate jejunitis Both of these diseases are extremely malignant the course is rapid and downhill and perforation and hemorrhage not uncommon (figs 57 and 58)

Continuous fever of intestinal origin arising in ileojejunitis or

ileitis must be recognized in the differential diagnosis where more common diseases of febrile nature receive first presumptive consideration Di eases characterized by continuous fever with low leukocyte counts include such syndromes as brucello is rheumatic fever periarteritis nodo a and lupu erythematosis di seminatu The advent of diarrhea o often overlooked or ignored indicates the po sibility if not the likeli hood of ileo jejunitis being the true cause of the febrile state (fig 70)



Fig 71 Sp ue—cha cte i t c segmentat on in loops of small bowel

Whipple s Disease

Avery Jones and Paulley called attention to the po ible relation hip of inte tinal granulomatous lipodystrophy and regional ileitis In te tinal lipodystrophy may simulate ileo-jejunitis and requires differenti ation from it This condition is characterized by a sprue like diarrhea



FIG 70 Same case as figure 66 two and a half years later subsidence of symptoms gain of fifty pound of we ght Absence of sten is and stricturing

Hodgkin s disease of the small bowel and diffuse multicentric sarcomatosis of the mesenteric lymph nodes with intestinal involvement are rare diseases which simulate jejunitis Both of these diseases are extremely malignant the course is rapid and downhill and perforation and hemorrhage not uncommon (figs 57 and 58)

Continuous fever of intestinal origin arising in ileo jejunitis or

examination In the duodenum the third and fourth portions occasionally also the second portion become thickened and rigid and converted into a semi rigid tube The periduodenal tissue and the pancreatic capsule may be inflamed and edematous The serosa is engorged and reddened and the regional lymph nodes are enlarged The microscopic picture as we have seen it in 2 cases has been compatible with that of granulomatous enteritis namely infiltration with plasma cell and fibroblasts with epithelioid and giant cell formation Fistulization between the stomach or duodenum and adjacent viscera is unknown as is perforation The clinical picture is dominated by obstruction

Almost always the local process in the stomach and duodenum is part of a more diffuse process involving one or more segments of the small bowel Occasionally the involvement of the duodenum represents an exceedingly high skip-lesion from an original focus in the distal or terminal ileum

In our present series we can add 4 more cases with involvement of the duodenum and 2 cases with nonspecific gastric lesions One of these 4 cases of duodenal involvement was acute in nature and was resolved without operation Radiographic examination a year later showed no evidence of the previous well marked disease In one case with involvement of the stomach a gastroenterostomy was performed with relief of symptoms In the second case of gastric and duodenal and jejunal involvement but without obstructions a two year follow up showed persistent symptoms on re x ray after two years the lesion in the stomach was no longer evident but the remaining lesions were unchanged

Clinical Symptoms

In the esophagus symptoms are dominated by sub ternal burning pain or heartburn with progressive dysphagia In the gastric cases Comfort has noted upper abdominal pains made worse by the ingestion of food with nausea vomiting diarrhea and progressive weight loss The vomiting and pain are the outstanding features Gastroscopy has shown diffuse superficial gastritis with multiple area of surface ulceration The gastric test meal is not unusual occult blood *in the fractional* specimens is usually present

In duodenal involvement obstruction is the *predominant* characteristic usually with protracted vomiting and rapid and extensive loss of nutrition and of electrolytes

and progressive loss of weight and strength associated with rheumatic and serous membrane manifestations It has been considered to be a collagen or connective tissue disease probably stemming from an underlying fundamental metabolic defect in the function of the intestinal mucosa A marked elevation of the serum glycoproteins exists with deposits of glycoprotein in characteristic foamy macrophages predominantly in the lamina propria and in the lymph nodes of the intestinal tract and of the body in general as typical granulomata The diagnosis can be established by a biopsy of the peripheral lymph nodes adenopathy occurring in about 50 per cent of the cases The disease is amenable to steroid therapy in many instances (Puite and Tesluk)

Primary Jejunal Ulcer

As an isolated phenomenon this entity has occasionally been described in the medical literature The lesion is usually located in the upper jejunum In several instance perforation followed trauma with acute peritonitis secondary severe anemia of such ulcers is not uncommon (Muehlbauer et al)

Granulomatous Disease of the Duodenum and Stomach

The increasing frequency with which a non specific pathologic disease of the duodenum and stomach is being recognized particularly as part of the picture of ileo jejunitis calls for special attention The literature has recently been thoroughly summarized by Richman Medical reports up to the year 1954 comprise 28 such well documented cases

In 1939 Shapiro reported 2 cases of regional enteritis involving the terminal duodenum and the proximal jejunum In the same year Ragnotti described a similar case In 1946 Menzel and Boving added 2 additional almost identical cases in addition to one reported by Janus In 1949 Ross described in detail an instance of involvement of the stomach small intestine and colon In 1950 Comfort et al added 3 new cases Eighteen additional cases have since been added to the literature making a total of 28 reported cases of involvement of stomach and duodenum and including one instance of the involvement of the esophagus (Carlisle and Judd Marten and Carr Anderson Mullinger and Bogoch)

In the cases in which the stomach was involved the posterior wall and greater curvature of the stomach were the usual site of the inflammatory process a mass resembling a small benign tumor may be felt and seen at the operating table and has been seen also by gastroscopic

examination In the duodenum the third and fourth portions occasionally also the second portion become thickened and rigid and converted into a semi rigid tube The periduodenal tissues and the pancreatic capsule may be inflamed and edematous The erosa is engorged and reddened and the regional lymph nodes are enlarged The microscopic picture as we have seen it in 2 cases has been compatible with that of granulomatous enteritis namely infiltration with plasma cells and fibroblasts with epithelioid and giant cell formations Fi tulization between the stomach or duodenum and adjacent viscera is unknown as is perforation The clinical picture is dominated by obstruction

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In duodenal involvement obstruction i the predominant characteristic usually with protracted vomiting and rapid and extensive loss of nutrition and of electrolytes

Radiologic Features

In the single case of esophageal involvement in the literature the distal third of the esophagus proximal to the lesion was somewhat dilated In the gastric cases the radiologic picture is one of pyloric or post pyloric obstruction without marked dilatation of the body of the stomach The duodenal bulb may be somewhat deformed though actual involvement of the first part of the duodenum has not been verifiably demonstrated The second portion of the duodenum may radiologically appear thickened and rigid but involvement of the Papilla of Vater *with jaundice has not been described The third and fourth portion of* the duodenum may be converted into a rigid tube with loss of haustral markings and with evidence of obstruction and narrowing proximal dilatation with stasis and with food residue exists A true string sign may occasionally be observed (fig 47 page 98)

Diagnosis

The diagnosis of the lesion when present in the esophagus stomach and duodenum usually depends upon the finding of concomitant lesion elsewhere in the small bowel However in 11 case in the literature the disease was limited to the stomach and duodenum

Treatment

The treatment of granulomatous disease of duodenum or stomach is usually surgical Medical treatment is purely symptomatic Gastro enterostomy will suffice to relieve the symptoms of obstruction in the duodenum more radical excision of involved segments is both impossible and unnecessary Again as in terminal ileitis a side tracking procedure is all that is required a transection isolating the diseased portion is not usually performed (Green)

Involvement of the antrum of the stomach particularly when hemorrhage is present calls for subtotal gastric resection Subsequent postoperative gastro jejunal ulcer has not been reported

Chapter 17 Malabsorption in Ileitis

by David A Turner Ph D *

The nutritional status of man on an adequate food intake depends on efficient digestion and absorption from the intestine Absorption is dependent first on digestion and secondly on the normal function of the mucosal cell In conditions characterized by abnormal secretion of digestive enzymes or impairment of the function of the intestinal mucosa varying degrees of malabsorption will occur

Malabsorption is not uncommon in patients with ileitis The degree of impairment of absorptive function is dependent on the anatomical distribution and the severity of the disease process However the marked nutritional disorders associated with malabsorption in the classical sprue syndrome are not usually so widespread in ileitis Evidence of impaired absorption may be so subtle that it can only be demonstrated with difficulty using special procedures In these individuals malabsorption may have little obvious clinical significance for many years On the other hand malnutrition resulting from malabsorption in some patients with ileitis may be sufficiently severe to be indistinguishable from that seen in sprue

Digestion and Absorption

The carbohydrates and starches must undergo complete hydrolysis (digestion) to their constituent monosaccharides before they can be absorbed The most important monosaccharides in human nutrition are glucose and fructose During their absorption the glucose and fructose molecules pass through the mucosal cell where they are phosphorylated to form a hexose monophosphate Phosphorylation provides for a constantly steep gradient in the concentration of these sugars from the intestinal lumen to the mucosal cell This provides for rapid absorption of these materials mostly independent of their concentration in the lumen The enzymatic removal of the phosphate moiety from the sugar occurs at the inner cell barrier Glucose itself is then liberated into the bloodstream

* D ct B chem t y R arch D Dpa tment of Med cine S a H p tal B lt m

The proteins undergo complete digestion in the lumen to their individual amino acids and in this form they are absorbed Little is known regarding the biochemistry of amino acid absorption The rapid rate of amino acid transfer across membranes can hardly be accounted for by passive diffusion it is probable that an active metabolic cycle is involved

The digestion and absorption of dietary fat remains a more complex matter and a problem of much controversy The classic view as presented by Verzar and McDougall (1936)* maintains that following emulsification in the intestine complete lipolysis or splitting of dietary fat into glycerol and fatty acids is necessary for absorption Thus glycerol is absorbed as a simple water soluble molecule and the fatty acids combine with bile to form water soluble complexes for absorption Within the mucosal cell the fatty acids combine with glycerophosphate in the synthesis of phospholipid in similar fashion to the changes involving glucose Dephosphorylation at the inner cell barrier results in the liberation of neutral fat into the systemic circulation Eighty per cent of absorbed fat is believed to be carried in the lymph to the thoracic duct there emptying into the bloodstream the remainder passes by way of the portal blood to the liver

More recently Frazer (1952) proposed the partition theory of fat absorption wherein some dietary fat is absorbed without preliminary splitting The partial hydrolysis of some triglyceride fat provides a fatty acid bile salt monoglyceride system capable of emulsifying other neutral fat into very fine particles less than 0 5 micron in diameter The finely emulsified neutral fat (triglyceride) is then absorbed through the intestinal mucosa into the lacteals and passes through the thoracic duct into the systemic circulation where it appears as chylomicrons On the other hand the fatty acids are partitioned from the neutral fat and it is claimed that they pass directly into the portal circulation to the liver

The degree of luminal degradation of dietary triglyceride to its constituent fatty acid and glycerol is the major point of difference between the *lipolytic* and th *partition* theories of fat absorption (see fig 72) The former theory postulates complete lipolysis while the *latter supposes liberation of only part of the fatty acid from the* triglyceride

*Bibliography for this chapter will be found at the end of the chapter page 197 199 All other references a[illegible] l[illegible]ted on page [illegible]0 235

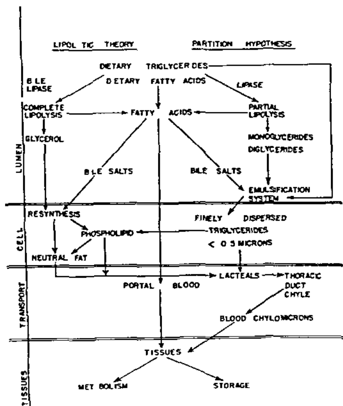


Fig 72 A hem h w ng th m la t es a d d ff nc b tw n th l p lyt nd p t t n the of fat bso pt on

At the present time on the basis of studies by Bergstrom and Borgstrom (1950) and by Reiser (1955) it would appear that complete lipolysis i improbable on the one hand and the absorption of triglyceride is unlikely on the other Actually partial hydroly i of all triglyceride to mono and diglyceride appear to be the preliminary chemical state necessary for the absorption of fat The resynthe is of these products to triglyceride within the intestinal cell remains unchallenged as does the lymphatic pathway a the major route of fat tran port to the systemic circulation

From the above it can easily be seen that abnormalities in digestion and subsequently absorption can occur with abnormal changes at various stages involving the digestive enzymes the luminal environment the integrity of either the structural or metabolic properties of the mucosal cell the lacteal and lymphatic transport system and finally the necessary physical contact between the mucosal cell and the products of digestion

Each of these possibilities can occur alone or in combination in patients with ileitis at various stages in the life history of the disease The absorption defects and their gross influence on the nutrition of the patient will be discussed below on the basis of personal experience and absorption studies carried out on some 200 patients with ileitis The effects of malabsorption will be considered as they may contribute to the clinical picture of ileitis

Gastrointestinal Defects and Malabsorption in Ileitis

Pancreas Dreiling (1957) found evidence of abnormal enzyme secretion of 8 of 26 ileitis patients subjected to secretion stimulation Only isolated enzyme deficiencies were observed and whether or not these were of sufficient severity to interfere with digestion is not known The incidence of impaired absorption is far greater in the case of fat than either carbohydrate or protein Whether this is indicative of a more complex mechanism for fat absorption or is merely a reflection of the larger molecular size of fat is not known Certainly dietary fat has a greater dependence on its hydrolytic enzyme pancreatic lipase than the other food stuffs for their particular enzymes When known diseases of the pancreas affect enzyme secretion abnormalities in fat digestion and absorption occur most readily even in the absence of evidence of carbohydrate and protein malabsorption

A relationship between pancreatic malfunction and the etiology of ileitis was first suggested by Avery Jones and Paulley (1949) and further elaborated upon by Cooke (1952) These authors observed certain similarities and relationship between sprue Whipple s disease and celiac disease (all characterized by steatorrhea) and ileitis They theorized that in the presence of altered lipolytic enzyme activity abnormal products of digestion could conceivably occur which might enter the mucosal cell and initiate the granulomatous lesion of ileitis A second possibility was based on the conclusions of Hass (1938) that multinucleated giant cell formation was a tissue reaction to interstitial lipolysis and liberation of abnormal fatty acids Thus some evidence

for abnormal pancreatic enzyme secretion has recently been found which may provide additional weight to the theory that abnormal fat digestion and malabsorption may be involved in the etiology of ileitis as well as a result of it

The Intestinal Mucosa The mucosal cell is the fundamental absorbing unit and as such it is a highly active metabolic entity The normal function of any cell is in part dependent on the maintenance of its structural component not excepting the cellular membrane and vascular supply The involvement of these structure in an inflammatory and cicatrizing lesion may result in their partial or complete physical destruction Under these condition the passage of materials across the cell membrane may not be possible if it does occur then their transfer through the interior of the cell in the absence of the normal eries of metabolic reacti n may be blocked Malabsorption at the cellular level would then result The pathologic proces of ileitis ha no limitation in the over all area of intestinal mucosa which may become involved Theoretically the infiltration of large areas of intestine with a destructive proces hould result in more severe impairment of cellular function and absorption than when mall areas are involved Thi is u ually found to be the case however it is not invariably true and the anatomical ites of the lesion as well a the stage in it life hi tory are contributing factors

Thu patient with large area of involvement and advanced disease have been tudied wh were presented with only minor absorption and nutritional difficulties These were u ually long-standing cases in whom it mu t be a umed that compen atory mechani m involving increased functi n f remaining normal ti ue through villu hypertrophy and delayed m tility had occurred On the other hand patient with mall area of inte tine involved in a highly inflammatory and active lesion with marked malabsorpti n have also been tudied

Th Site f Ab rpti n The anatomical ite of the lesion may also play a maj r r le in determining he extent of malabsorption Evidence ha been reported which indicates the exi tence of defined length of inte tine with pecialized cell f r absorbing one material or another In 1936 Verzar and McDougall observed that glucose wa preferentially absorbed fr m the proximal half of the small intestine Mollin (1957) and hi w rker in England ha e demonstrated in the rat that the ileum i the primary ite of absorption of Co[60] labeled vitamin B Thi i in agreement with clinical observation of impaired absorption of B

From the above it can easily be seen that abnormalities in digestion and subsequently *absorption can occur with abnormal changes at various* stages involving the digestive enzymes the luminal environment the integrity of either the structural or metabolic properties of the mucosal cell the lacteal and lymphatic transport system and finally the necessary physical contact between the mucosal cell and the products of digestion

Each of these possibilities can occur alone or in combination in patients with ileitis at various stages in the life history of the disease The absorption defects and their gross influence on the nutrition of the patient will be discussed below on the basis of personal experience and absorption studies carried out on some 200 patients with ileitis The effects of malabsorption will be considered as they may contribute to the clinical picture of ileitis

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presence of the actual di eased ti sue may be eliminated In time following resection the absorption of carbohydrate and protein (and often fat) is partially or totally restored even when several feet of intestine have been removed Compensatory mechanisms appear to be responsible for this restoration of function (Kogan Schapira Janowitz and Adlersberg 1957) The personal experience of the present author following removal of all but five feet of small intestine has been a persi tent intolerance to fat and fat soluble vitamins but normal absorption of carbohydrate protein water soluble vitamins (except B) and electrolytes

Hypermotility Malabsorption may occur in the presence of marked hypermotility as ociated with active disease limited to a very small portion of the total absorbing mucosa The cause of impaired ab orption in these instances is based on insufficient contact time between the intestinal mucosa and the material to be absorbed The deficiencies observed under these conditions are not usually limited to single entities but cover the broad spectrum of the diet since the entire food bolus is passing through the length of the intestine at a rate too rapid for any of its constituents to have sufficient contact time with the mucosal surface to be absorbed

The Measurement of Malabsorption

The oral tolerance te t has been the procedure most widely used to study absorption from the inte tine in ileitis This method involves the determination of the concentration of a test sub tance in the blood or urine after an oral test dose of that substance or its precursor

The interpretation of a tolerance test as a measure of intestinal absorption requires some degree of caution The blood concentration is the resultant of absorption utilization and mobilization from storage depots and is not merely a measure of absorption alone In addition the results of a tolerance test utilizing a single test substance must be expressed in terms of the material fed rather than in term of over all absorptive function since the intestine varies in its capacity to absorb different sub tances particularly under abnormal conditions

The use of balance studies in which the quantitative estimation of intake and output is performed is probably the most accurate means for studying absorption The cost of the special facilities necessary for such studies has limited their use

Recently radioactive isotope labeled materials have become readily available and these have stimulated new interest in the possibility of

in patients in whom the ileum has been surgically removed In 1954 Kremen Linner and Nelson carried out fat balance studies in dog after removal of distal or proximal lengths of intestine from gastrointestinal continuity Their studies indicated that steatorrhea and weight loss was greater with removal of the distal small intestine they concluded that the distal small intestine was the major site for the absorption of fat Benson (1956) and his group fed I^{131} labeled olive oil to rats and found that a specific portion of the third quarter of the mucosa of the jejunum contained the maximum activity Turner (1956) fed both dogs and rats I^{131} and C^{14} labeled neutral fats and observed a maximum activity of labeled fat from the duodenum beginning at the ampulla of Vater and continuing to the distal jejunum (fig 73) These observations were in agreement with the early reports of Claude Bernard (1856) who described the occurrence of milky chyle after a fatty meal immediately distal to the ampulla of Vater in dogs and rabbits These results appear to be in conflict with those reported both by Benson and by Kremen However it seems difficult to relate their findings to the frequently reported observation of maximal lymphatic lactescense indicative of fat absorption in the proximal intestine after a fat meal The clinical significance of these findings is presently being investigated in this laboratory with patients undergoing resection at various levels of the small intestine

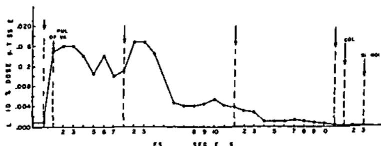


FIG 73 The residual I lipid activity in serial sections of the gastrointestinal tract 3 hours after the ingestion of 20 Gm I triolein

Resection of portions of the small intestine in ileitis results in the reduction of effective absorbing mucosal tissue Basically the effect is similar to that observed when similar areas of the mucosa are destroyed by the disease process although certain secondary effects due to the

presence of the actual diseased tissue may be eliminated In time following resection the absorption of carbohydrate and protein (and often fat) is partially or totally restored even when several feet of intestine have been removed Compensatory mechanisms appear to be responsible for this restoration of function (Kogan Schapira Janowitz and Adlersberg 1957) The personal experience of the present author following removal of all but five feet of small intestine has been a persistent intolerance to fat and fat soluble vitamins but normal absorption of carbohydrate protein water soluble vitamins (except B_{12}) and electrolytes

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Recently radioactive isotope labeled material have become readily available and these have stimulated new interest in the possibility of

obtaining quantitative measurement of intestinal absorption utilizing specific substances in oral tolerance tests

Carbohydrate Absorption The glucose tolerance curve is not very useful as a measure of absorption in these cases because of its marked dependence on other variables such as liver adrenal and pancreatic function No diagnostic features were noted using this procedure in 112 patients with ileitis The results in 85 per cent of the cases were within normal limits but considerable variability was observed in any one individual tested on several occasions The rapidity with which glucose is absorbed from the upper small intestine (Verzar and McDougall 1936) apparently assures normal absorption except where malfunction involves the whole intestinal mucosa such as in sprue

The use of the pentose sugar d(+) xylose as the test substance has provided a more consistent means for studying absorption (Brien Turner Watson and Geddes 1952) The resultant curve in 100 normal subject and in 60 patients with ileitis studied was highly reproducible on separate occasions in the same individual In the abnormal group deviation of the test curve from the normal mean was usually closely related to the

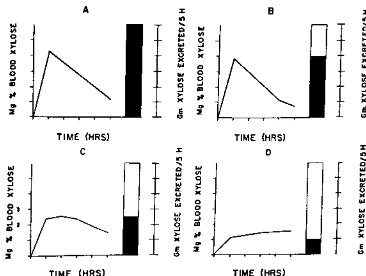


FIG 74 The characte tic blood xylo e changes and ur ne xylose e cretion following the ingest on of 25 Gm of D(+) xyl e n (A) normals (B) regional ileitis (C) ileo jeju t and (D) sprue

extent of pathologic involvement of the intestinal mucosa as determined at operation or by roentgen examination

The sensitivity of the test to changes in absorption was highly significant a flattened blood and urine test curve often preceded gross clinical or roentgen evidence of the disease process The procedure has gained wide acceptance as a single diagnostic screening test for conditions such as sprue celiac disease and ileitis Its particular value lies in differentiating borderline malabsorption where overt clinical evidence is not yet evident (figs 74 and 75)

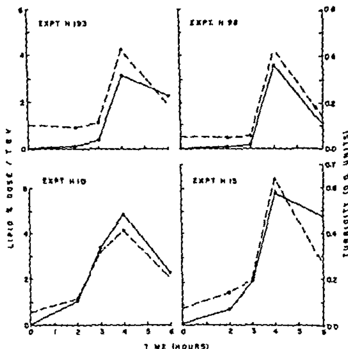


Fig 75 Th plasma lipid act vity (———) and O D (— —) changes in 4 n mal human aft the nge t n f a 40 Gm 1 triol n meal

The starch tolerance test has greater value as a measure of adequate carbohydrate digestion than as a measure of intestinal absorption The procedure involves the oral administration of the polysaccharide (starch)

obtaining quantitative measurement of intestinal absorption utilizing specific substances in oral tolerance tests

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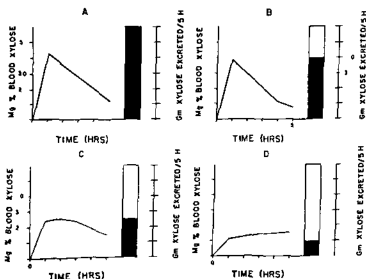


Fig 74 The characteristic blood xylose changes and urine xylose excretion following the ingestion of 5 Gm of D(+) xylose in (A) normal (B) regional ileitis (C) ileojejunitis and (D) sprue

of calculated total fat intake This is in contrast to the older 12 day pooled stool collection program and the fractional determination of fecal fat content

By this method 90 per cent or more of dietary fat is normally absorbed Steatorrhea occurs when less than 85 per cent of the fat intake is absorbed The contribution of endogenous fat to the fecal fat content cannot be adequately determined by this procedure and the role of such fat in the etiology of steatorrhea remains a point of controversy

In ileitis the fecal fat content is elevated beyond normal limits in a majority of cases Cooke (1955) observed steatorrhea in 45 of 57 cases studied by this technique In nonoperative patients with involvement of the jejunum or upper ileum steatorrhea was invariably found When the disease was limited to the distal ileum in the one patient from whom 5 feet of distal ileum had been removed there was no evidence of steatorrhea Thus impaired fat absorption does not necessarily follow resection of certain areas of the small bowel These findings lend considerable support to the observation that the ileum plays a minor role in the normal process of fat absorption

Fat Tolerance Tests Butter fat olive oil and other dietary fats have been orally administered and the changes in the plasma lipid concentrations chemically determined The large volumes of blood necessary and the time consuming chemical analyses involved make this technique impractical for repeated serial testing in most instances This type of fat tolerance test is rarely employed at the present time

Vitamin A The vitamin A tolerance test has been the most popular measurement of fat malabsorption because of its consistency and simplicity This has been further stimulated by the work of Legerton Texter and Ruffin (1953) who showed a direct correlation between fat absorption and vitamin A absorption Adlersberg and Sobotka (1943) reported little impairment of vitamin A absorption in ileitis in contrast to sprue where the tolerance curve is usually flat Kogan et al (1957) found that the vitamin A tolerance curve was fairly normal in several patients following massive resection but this was not consistent The vitamin A tolerance curve as an index of fat absorption should be read with some caution in the absence of other measures since it does not always follow the fat absorption pattern

Radioactive Labeled Fats Radioactive iodine (I^{131}) labeled fat have been shown to be absorbed in similar fashion to ordinary unlabeled fats and a method has been developed for their rapid and simple measure

followed by measurement of the changes in blood glucose concentration Galactose has also been used as the test substances in these procedures but this has doubtful advantages over glucose

Protein Absorption The amino acids are readily absorbed under all but the most abnormal conditions and their use in oral tolerance tests has not been very informative Nitrogen balance studies provide the best means for studying protein absorption Glycine is easily measured in blood by a simple colorimetric technique and it has been used clinically in a tolerance test In 50 cases of ileitis and in 42 patients with partial gastrectomy little consistent evidence of impaired glycine absorption was observed Even in sprue with evidence of gross malabsorption the glycine tolerance curve was often within normal limits The oral administration of gelatin with subsequent determination of the changes in blood glycine concentrations has some value in the study of pancreatic (trypsin) function but is of little specific value in studying absorption from the intestine

Ruffin (1956) and his colleagues have employed I^{131} labeled albumen for this purpose with some success Radioisotope methods are more convenient than chemical methods when properly used but the labeled proteins presently available that could provide valuable information on protein absorption have not been appropriate for widespread human application

Fat Absorption The measurement of fat absorption has been the subject of intense interest in recent years The reason for this is probably two fold steatorrhea has become increasingly important as an early and troublesome complication in diseases of the intestine Quite recently quantitative and convenient investigative procedures which were previously lacking have been developed to study fat absorption in man The great vacuum which existed in our knowledge of fat absorption and metabolism in man was a direct result of this paucity of adequate methodology

The availability of radioactive labeled fats on the one hand and improved chemical and physical analytical procedures on the other now make possible certain human studies which were previously limited to animals

Fat Balance The method of Van de Kamer (1949) and his group for measuring fat absorption by the balance technique represents a distinct improvement over older procedures Here the stools are collected on a 24 hour basis and the total fatty acid content measured by a rapid and simple chemical procedure The results are expressed as a percentage

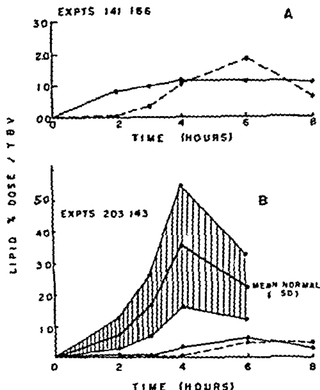


Fig 76 Th I[131] t i l m t lerance cu es n pat nt afte (A) e ecti n of 3 fe t of t rminal l um f t m nal l t and (B) aft res ction of the ent e l um f r d ff e ile tis and the m an normal cu v (± S D)

re ection the 48 hour stool values were 19 per cent and 31 per cent of the dose

The results using chemical analysi of fecal fat or I triolein levels are comparable the latter may well serve a a simplified sub titute for tedious chemical analyses or as a supplement for confirmation of special studies

I -oleic acid has been u ed in similar fashion to triolein as a means of *differentiatin*, steatorrhea due to intestinal (mucosal) disease The I -oleic acid tolerance curve is es entially normal in pancreatic steatorrhea while that of I triolein is not In ileitis or sprue with steatorrhea *neither* the I oleic acid nor the triolein curves reaches

ments in small volumes of plasma (Turner 1956) The I^{131} triolein and the I^{131}-oleic acid tolerance tests have been used to study fat absorption in 92 patients with steatorrhea resulting from ileitis (46) pancreatic insufficiency (42) or sprue (4)

The measurement of an isotope like I^{131} has many advantages over conventional chemical procedures including greater accuracy and simplicity of determination In addition any increment in the I^{131} lipid levels in the plasma can be definitely attributed to the administered material in contrast to the use of material indistinguishable from endogenous tissue lipids

The normal mean I^{131} triolein blood tolerance curve reaches a maximum value of 4 to 6 per cent of the administered dose per total blood volume in 4 hours (fig 75) In 46 ileitis patients the value rarely exceeded 1 2 per cent In each of 8 patients with previous resection of portions of the ileum the I^{131} triolein tolerance test was repeated on three occasions The maximum peak was consistently less than 1 per cent (fig 76) Subsequently each of these patient underwent further surgery for recurrent disease

The invariable finding of impaired ab orption of I^{131} triolein in ileitis may not be a true reflection of the patient s capacity to absorb dietary fat Weijers and Van de Kamer (1950) showed that saturated fatty acids may be selectively rejected by the abnormal intestine while unsaturated fatty acids may be well ab orbed even in steatorrhea When triolein is labeled with I^{131} the unsaturated bonds of the constituent fatty acids (oleic acid) are saturated by the halogenation Nevertheless the procedure as outlined and under these conditions is a sensitive method for measuring fat absorption

The fecal fat level of I^{131} triolein vary inversely as the blood levels after the I^{131} triolein test meal When the tolerance curve is depressed the fecal activity is high Some workers have preferred to measure the fecal I^{131} triolein activity and this has certain advantages The limitations in the meaning of a blood tolerance curve are overcome and in addition the sample may be measured directly without previous preparation On the other hand fecal studies involve stool collections which are not always possible or practical

McKenna Bourne and Matzko (1957) have compared both blood and fecal I^{131} triolein level in normals and in patients with steatorrhea They found less than 4 per cent of the ingested labeled fat in the 72 hour stool of normal subjects In two ileiti patients with previous

of its long half life The availability of a short lived calcium isotope would be a valuable aid to such studies

Effects of Malabsorption

Malabsorption is normally a subtle symptom in the majority of patients with ileitis However subtle deficiencies of this nature result in gross effects if they are not corrected or compensated for over long periods of time

The systemic effects of malabsorption may be resolved under the heading of malnutrition In ileitis the picture is one of chronic progres ion of these effects in terms of their severity and anatomic distribution In addition individual deficiencies and malfunction tend to become further complicated when they give rise to secondary disturbances in a cause and effect relationship For example even if protein absorption is normal the presence of steatorrhea may result in weight and energy loss and the breakdown of the protein sparing mechanism and secondary protein deficiency by the conversion of dietary protein to fat and carbo hydrate for metabolic purposes Unless sufficient carbohydrate and protein are fed under these conditions the depletion of existing tissues coupled with impaired synthesis of new ti sues will re ult in a disastrous chain of events

Impairment of fat absorption is the mo t common form of mal absorption observed in ileitis The loss of fat soluble vitamins A D K and E may result in any of the known clinical entities peculiar to their deficiency

Electrolyte disturbances are usually associated with potassium or calcium loss in these patients Thus generalized muscle atonia and tetany respectively have been observed in certain instances Osteomalacia associated with calcium lo s secondary to protein depletion and vitamin D loss with steatorrhea has been reported

With watery diarrhea and the consequent loss of the water soluble vitamins the classical signs of B complex deficiency are commonly observed These can be adequately controlled by appropriate parenteral therapy

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normal levels The defect in pancreatic deficiency is in lipolysis which only affects triglyceride whereas the defect in ileitis and sprue is a fundamental absorption defect at the cellular level

Vitamin B_{12} Absorption The absorption of vitamin B_{12} has been studied by three techniques all of which confirm the widespread impairment of vitamin B_{12} absorption in ileitis and particularly in the presence of steatorrhea Again the use of radioactive labeled material $Co^{60}B_{12}$ has simplified and extended clinical studies of intestinal absorption

Heinle Welch Scharf Meacham and Prusoff (1952) gave 0 5 μg doses of $Co^{60}B_{12}$ and measured the fecal excretion of radioactivity The method of Schilling (1953) involves the administration of 5 μg *of $Co^{60}B_{12}$ followed by a parenteral injection of 1000 μg of non* radioactive B_{12} If the $Co^{60}B_{12}$ has been absorbed considerable radioactivity can be measured in the urine whereas none will appear if it has not been absorbed More recently Glass Boyd Gellin and Stephanson (1954) have shown that $Co^{60}B_{12}$ taken by mouth accumulates in the liver and that the radiation can be counted by directional scintillation counting over the liver

The method of Glass et al (1954) appears to be the most practical procedure with which to study vitamin B_{12} absorption in patients with malabsorption To differentiate vitamin B_{12} malabsorption in pernicious anemia from that observed in sprue or ileitis a source of intrinsic factor is given with the test dose of $Co^{60}B_{12}$ In pernicious anemia the B_{12} will be normally absorbed under these conditions but intrinsic factor has no effect on the absorption of vitamin B_{12} in intestinal disease

Damage to the mucosa of the ileum by disease or its surgical removal would be expected to result in vitamin B_{12} malabsorption since the ileum appears to be the site of vitamin B_{12} absorption

Electrolyte Absorption The presence of steatorrhea or watery diarrhea results in the loss of electrolytes in the stool This phenomenon has been intensively studied by Cooke (1955) who found that potassium loss was the most significant observation The fecal determination of these elements remains the best method for determining their absorption The use of radioactive K has not been completely satisfactory in terms of a tolerance test using this isotope

Ca^{45} has been used in this laboratory in studies of the absorption of calcium in dogs with experimental steatorrhea Fecal calcium loss is increased markedly in the presence of steatorrhea The use of this isotope in human subjects is not compatible with present safety regulations because

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Chapter 18 Prognosis and Treatment of Ileo-Jejunitis

OF THE 70 CASES in this present series 50 were followed for from 1 to 25 years unfortunately 20 were lost to follow up Even so it might be interesting to see what happened to those successfully followed

TABLE 18

FOLLOW UP OF MEDICALLY TREATED CASES (32 CASES)

Years	*Good*	*Poor*	*Died*
0 1	3	2	
1 2	1	1	4 deaths (medical)
2 3	0	1	directly
3 4	3	1	attributable
4 5	3	0	to the disease
5 10	7	2	
10 15	3	0	
15 20	0	0	
20 25	1	0	
	—	—	
	21	7	

TABLE 19

FOLLOW UP OF SURGICALLY TREATED CASES (18 CASES)

Short circuiting procedure	1 case	poor result
Resection	4 cases	good result
	9	poor
	4	deaths

All deaths occurred immediately postoperative

Obviously surgery has little place in ileo jejunitis except as an emergency procedure for obstruction Attempts at massive resections are disappointing and are associated with a high operative mortality Four cases that survived massive resection were well and were not showing electrolyte imbalance despite small segment of persisting jejunum On the other hand medical conservative treatment is most promising with a high percentage of improvement and with restitution to fair health and good efficiency

In 1941 Crohn and Yunich published a series of 38 cases of ileo jejunitis 13 of which were well 6 clinically in fair condition 7 poor 6 deaths and in 6 no follow up It would seem then that our latest the present (1957) series shows better end results possibly due to the extensive use of the steroids A typical case is that of a young man 17 years of age who was being observed for ileo jejunitis with diffuse involvement of the jejunum and upper ileum with active symptoms Five years later a follow up showed marked clinical improvement cessation of active symptoms and a gain of 50 pounds in weight On re x ray the jejunal pattern was seen to be restored to normal the upper ileum was contracted the mucosal pattern disarranged thus indicating the greater susceptibility of the upper jejunum to self healing This observation has been repeatedly made in this series namely clinical cure though persistent radiographic evidence of a burnt-out disease

Such instances of apparent cure of jejunitis confirmed by exploratory operation or by roentgenography have previously been independently noted by Pessagno by Wilensky by Sussman and Wachtel and by Kross in individual cases

On the other hand the severity of the disease is indicated by the fact that in this series 7 cases were only fair or poor and above all 4 had fatal terminations as a result of perforation (1 case) of sepsis (Friedlander bacillus) (once) of inanition (1 case) of intercurrent disease (1 case) The unsatisfactory clinical outcome in 7 cases including 4 deaths is clear evidence of the severity and persistence of the disease process in progressively undermining nutrition and protein and mineral reserves

The fact that 21 cases did improve sufficiently as to resemble clinical cure is impressive and does indicate that self healing in high jejunitis is possible The regain of weight in these cases is impressive and the surcease from fever diarrhea and anemia most striking

Medical Therapy

The conservative treatment of ileo jejunitis applies principally to the type in which diffuse involvement of the entire small bowel exist or to those in which the disease affects such large stretches of upper ileum and the whole jejunum as to preclude any idea of surgical intervention The conservative approach to therapy is aimed at establishing some degree of partial sterilization of the intestinal tract by the use

of antibiotics and to maintain nutrition and electrolytic balance in the plasma and to combat anemia and vitamin deficiencies

As antibiotics penicillin is useless streptomycin is possibly of some avail In the febrile cases particularly where suppurative complications mesenteric abscess and fistula or perirectal manifestations are suspected the broad spectrum antibiotics are of greatest utility It is difficult to say which of these antibiotics gives the best re ults if there is actually any true basis for preference Aureomycin and terramycin should not be employed because of their tendency to increase the severity of the diarrhea by suppressing the normal flora of the intestinal tract Achro mycin erythromycin Mysteclin disturb least and give better results it is quite po ible that one of the newer broad spectrum antibotics of which there seems an unending list will surpass others in reducing fever and secondary infection without producing untoward intestinal side effects

The corticosteroids offer the best approach to direct therapy over a long period of time ACTH by injection is rarely needed except in febrile cases cortisone hydrocortone or meticorten or predni one given by mouth in doses of 15 to 25 milligrams daily over long periods is best indicated These dosages seem small in comparison to the dosage employed by many other clinicians In fact we have seen cortisone or its analgous products given in dosage of up to 75 to 150 milligrams daily and according to these authors with excellent results One of the best cases we saw one of diffuse ileo jejunitis with complete resti tution to health and efficiency was maintained on this high dosage for many months It is our own view that the dosage should be more mod erate much more so but prolonged over months and if necessary years

Nutrition is maintained by a liberal soft nonroughage diet not too strictly construed High protein high carbohydrate elements in the diet are stres ed meats fi h chee e egg milk pureed vegetables fruit juices and bread and butter being forced (see pp 122 124) The protein content of the diet may be reinforced by the use of the protein hydroly sates up to 4 to 6 ounces a day being urged on the patient The newer commercial preparations are no longer bad tasting they are actually palatable and tend to maintain and re tore nitrogen balance Occasional transfu ions of whole blood or of plasma aid in overcoming hypopro teinemia rai e the total proteins of the blood and restore when plenti fully administered over a long period of time the relationship between the albumin and globulin factions of the plasma

The intramuscular injection of crude liver extract plus vitamin B

complex 2 cc of each plus B 50 micrograms every day or every other day tend to overcome anemia encourages blood formation and replaces the deficiency in vitamin absorption which re ult from the damaged intestinal tract Even though the beneficial effect of such injection are not evident in ileo-jejunit as in prue they hould continue to be regularly admini tered

Fresh air sun hine and much re t particularly at the sea hore or in the mountain often act beneficially to effect general improvement in weight and strength

Surgical Intervention

The indication for surgical interference are limited to those cases in which the lesion i localized to one or more isolated segments of the small bowel such as group 1 and 2 possibly and group 6 more likely (see chapter 16 page 160)

In thi series of 70 cases 18 were subjected to a radical procedure The follow up of these cases has already been noted in table 19 A wa observed good result were obtained in only 4 ca es 4 additional death and 9 poor results certainly do not erve a encouragement for radical surgery in ileo jejunit And yet surgical intervention i warrantable and indicated when the true nature of the disea e i in doubt or the extent and implication of the di ease cannot be radiographically estab li hed with certainty or where the question of ob truction has been raised A case may seem to be segmental or localized in extent but at exploration may be di covered to be of the diffu e type not amenable to resection Or a case con idered diffuse and probably incapable of surgical help may be determined at exploratory operation to be egmental and capable of resection

Where no benefit i being derived from con ervative medical treat ment an exploratory operation i often justified The removal of the appendix i a superfluou manipulation fortunately in ileo-jejunitis appendectomy rarely result in abdominal wall fi tula

In group 1 where the disease i an extension upward of ileiti so a to invade and include the jejunum radical urgical procedure offer scant hope of success

In group 3 4 and 5 those cases in which the di ea e invades the whole of the jejunum and much or all of the ileum the ame di cour aging attitude toward reckless exci ion of the involved intestine hold equally true

Massive resection of the mall bowel with the sacrifice of most

of its length has been occasionally encountered in the literature not for ileitis or jejunitis but more often for strangulation for volvulus for superior mesenteric vein thrombosis or for intus usception (Cop well Gorse)

The average length of the small intestine varies under normal con ditions from 18 to 26 feet averaging 21 feet 6 inches

Gray s Anatomy—20 feet 6 inches

Rost—18 to 26 feet averaging 19 feet

Treve —22½ feet in the male 23¼ feet in the female adult

Sarnoff felt that half of the small intestine could be sacrificed with out unduly endangering life and he quoted 5 cases in which 18 17½ 17 16 and 13¼ feet of small bowel had been removed all survived the operation but died later Pate reported a case in which 12½ feet of small bowel were removed for a traumatic strangulation of the mesen tery only 12 inches of jejunum remaining the patient was well four weeks later In a case reported in 1940 (Todd Dittenbrandt and Mon tague) all but 3 feet of jejunum had been surgically removed resultant carbohydrate metabolism was normal proteins not so well absorbed (67 75 and 76 per cent in three periods) tetany was prevented by liberal administration of calcium and vitamin D In their study of metabolism in the cases 25 per cent of the protein intake and 45 per cent of the fat intake were lost in the feces a total loss of 25 per cent of the calorific value of the inges ed food The fecal fat showed much free fatty acids indicating good splitting but poor absorption

Coleman and Bennett report massive small intestinal resection with survival the resection involving 6 feet 7 inches in one case 14 feet 8 inches of small bowel in another case Prioleau also supports the view that massive resection of the small intestine is possible with survival under fortunate circumstances He reports 2 cases one with a 40 per cent resection and one with a 53 per cent resection of the small bowel with survival although the latter case died four months later Elman and Reed report the resection of all but 3 feet of proximal jejunum and also the right half of the colon the patient gained 50 pounds of weight and experienced normal bowel function The results of human resections indicate that approximately two thirds of the small bowel can be removed without serious risk of life (Berman et al) They report the removal of all but 18 inches of the jejunum and the right half of the colon for ergot poisoning and superior mesenteric vein thrombosis with complete recovery the daily postoperative defecations were limited

to three formed stools per twenty four hours Althausen reported the resection for mesenteric thrombosis of 435 cm of the jejunum The patient survived the operation tolerably well with retained nutrition as proved by extensive studies of metabolism and of food absorption

While such massive resection of the small bowel are thus shown to be possible with survival the attempt to apply that principle to diffuse ileo-jejunitis would likely be associated with an extremely high mortality because of the previou state of malnutrition and anemia and is scarcely to be encouraged

In group 6 tho e cases with high and isolated segmental involvement of the jejunum localized resection of the lesion is not only possible but is highly successful Such was the outcome in our 3 cases in thi present series Johnson resected 3 feet of upper jejunum beginning at the fos a of Treitz for localized jejunitis Brew ter resected 2 feet of jejunum for a lesion beginning 2½ feet caudad of the fossa of Treitz Both cases made complete recoveries Spellberg and Gray performed a gastroenterostomy for a traumatic segmental jejunitis because of poor result denoted by delay in the proximal loop a secondary resection was performed with a succes ful outcome Gendel and Beaver had an identical experience Lyons and Garlock resected 10 inches of upper jejunum for localized jejunitis whose upper limit was the fossa of Treitz with good result The case of Koenig was equally successful after a resection of 3 feet of jejunum

In high jejunitis multiple segments of involvement are not un common It often becomes necessary to treat or resect each individual focus of disease as an independent lesion in order to achieve a successful outcome Dixon cites a striking case of recurring obstruction from multiple non neoplastic tumefaction of the jejunum An interesting in sight into the life hi tory of localized jejuniti may be gained from the study of a case publi hed by Husebye In 1928 a 49 year old man was operated on for an acute phlegmonous jejunitis an entero- anastomosis was performed at the ileo-jejunal junction The operation wa followed by a long period of apparent good health In 1945 or seven teen years later the reappearance of heartburn and abdominal cramps was followed by the clinical picture of an acute abdomen The radiographic examination showed the upper jejunum to be irregular nar rowed tortuous the upper jejunum and the duodenum were distinctly dilated and retained barium At operation the roentgenographic findings were confirmed the jejunum was diffu ely scarred the lumen contracted

and the proximal bowel and duodenum and stomach abnormally dilated A gastro jejunostomy and a jejuno jejunostomy were performed the patient succumbed to the high intestinal obstruction and the extensive surgical procedures Apparently in this case in spite of the entero-anastomosis the healing of the short circuited segmental jejunitis had resulted in scar tissue contraction and in high intestinal obstruction

In group 2 where a high jejunitis is associated with an independent and similar lesion in the terminal ileum the operation of choice is localized resection of the upper jejunal lesion and a short circuiting of the lower ileal lesion (ileo transverse colostomy with transection of the proximal ileum above the diseased area) Our previous (1949) series included three instances of combined lesions successfully operated on by local resection of the terminal ileal segment all of them successfully accomplished

In summary it will be seen that surgical intervention in ileo jejunitis is advocated both as an exploratory procedure and as a means of attack in those cases of high jejunitis with or without distal ileal involvement In the localized or segmental forms of jejunitis surgical intervention results frequently in restoration of health and intestinal function

Chapter 19 Ileocolitis

by Harry Yarnis, M.D.*

Both ileitis and nonspecific or idiopathic ulcerative colitis constitute allied diseases and, if not identical in nature, at least belong to the same family. The etiology of neither disease is known; both occur in young people and have the same sex distribution; both have the same general life span of extension with recurrences and are characterized by such common complications as rectal suppurative phenomena, erythema nodosum, fever, hypoproteinemia and secondary anemia. Both occur in the pure form in the great majority of cases, but certain mixed forms must be recognized. Thus universal ulcerative colitis will involve the terminal portion of the ileum in about 25 per cent of the cases. Segmental or right-sided ulcerative colitis will involve the terminal ileum in a much higher number of instances, Crohn, Garlock and Yarnis having reported involvement of the terminal ileum in 40 per cent of 77 cases of segmental colitis. The ileitis in these cases is not granulomatous in nature but ulcerative or exudative in type, and is due to regurgitation of the infected colonic contents through an incompetent ileo-cecal valve. Such ileitis does not extend aborally by skip-lesion, does not cause obstruction and is not associated with internal or external fistula.

On the other hand, true regional enteritis infrequently crosses the ileocecal valve. However, only two years after the original description of terminal ileitis in *1932 Colp* published a report of a case in which he resected a nonspecific granuloma of the terminal ileum and cecum. Subsequently similar cases were added, and in 1936 Crohn and Rosenak cited 60 cases of regional ileitis, in 9 of which simultaneous involvement of the colon was found to exist. Musick further described a case in which 18 inches of ileum, 3 inches of cecum and 3 inches of sigmoid were simultaneously involved. An ileo-ascending colostomy was performed on the right side, Mikulicz procedure on the left colon, with successful outcome. Pessagno (1937) reported regional ileitis with in-

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volvement of the cecum Pugh reported 9 cases of ileitis with evidence of extension of the pathologic process into the large bowel In 6 the cecum in 2 the sigmoid and in one the transverse colon were implicated The parenthood of the combined form of the disease seems to rest in the terminal ileum Pemberton and Brown pointed out that if an ileocolostomy be performed for a combined lesion at subsequent exploration the colonic lesion will be found healed only the ileitis constituting the residual focus of the disease This is an astute observation which is amply confirmed in the life histories of several cases in this present series Clark and Dixon found that in 23 out of 44 cases of regional enteritis ob erved the large bowel mainly cecum and ascending colon were involved with the terminal ileum And yet they distinctly say The distal portion of the ileum appeared to be the original site of invasion of the disease in practically all cases

The highest incidence of colonic involvement in regional ileitis was reported in 1951 by Rappaport Burgoyne and Smetana who published a report of 100 cases of regional ileitis with extension into the colon in 55 instances However in many of these cases the granulomatous extension into the colon was minimal and could be detected only by mic ro copic technique In our personal experience granulomatous involvement of the colon in regional ileitis has not been common However minimal involvement of the cecum and ascending colon by granulomatous disease is frequently secondary to internal fistulas which originate in the diseased ileum and terminate in the colon

The granulomatous nature of regional ileitis and the inflammatory character of the typical ca e of ulcerative colitis are well established However there is no such agreement concerning the pathology of segmental or regional colitis Warren and Sommers regard these two diseases as morphologically different and have never seen a case of granulomatous colitis On the other hand Newman and Dockerty reported 25 resected specimens of egmental colitı in which there was a marked thickening of the entire colonic wall and microscopically presented as nonspecific granulomatous process Wells reported cases of segmental colitis in which he described the typical microscopic appearance of a granuloma with giant cells and epithelioid tubercle formation in the colon In fact the gross and microscopic appearance in these ca es of segmental colitis was so similar to granulomatous or regional ileiti that he chose to call this type of segmental colitis Crohn s disease of the colon

Brooke and Cooke described a form of ileocolitis due to malabsorp tion and dysfunction of the small intestine resulting in poor fat absorp tion and steatorrhea This is followed by superficial ulceration of the ileum which progresses through the ileo cecal valve to involve the colon It is necessary to recognize this type of deficiency disease because surgical intervention is precluded due to the progressive nature of the malady

In our experience the pathologists have almost always reported re sected specimens of segmental colitis as ulcerative in nature However in the past two years we have seen 4 cases of typical granulomatous dis ease of the colon In all these cases there was marked thickening of the colonic wall in many instances there were skip areas and the micro scopic appearance revealed fibrosis giant cell system and epithelioid cells or tubercles

Therefore it appears that regional ileitis may be associated either with ulcerative colitis or with granulomatous colitis The term com bined ileocolitis means the pre ence of granulomatous ileitis and ulcer ative colitis When granulomatous ileitis combines with granulomatou colitis the best term we believe i granulomatous ileocolitis







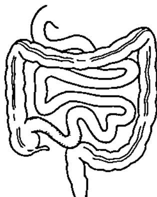


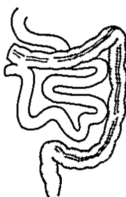


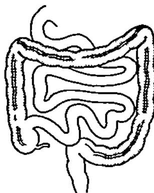


Fi 77 Ileocol t n tomical d t b ti n— ynch ous type

Furthermore the combinations of these two diseases may take place simultaneously (synchronous) or may occur in sequence (metachronous) Thus if ileitis is designated as E and ulcerative colitis as C and granulomatous colitis as G the following variations may occur EC synchronous combined ileocolitis EG synchronous granulomatous ileocolitis E plus C primary ileitis to which ulcerative colitis is later added and C plus E ulcerative colitis that is later complicated by ileitis







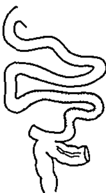


Fig 78 Ileocolitis metachronous type

Our present study includes 64 cases of ileocolitis[3] Of these 60 represent combinations of true granulomatous ileitis and various forms and distributions of ulcerative colitis There were 4 cases of granulomatous ileocolitis In 41 case both ileitis and ulcerative colitis were present at the onset of the disease so that the combined ileocoliti wa synchronous in origin In 19 ca es either ileitis or ulcerative colitis wa originally present but after an attempt to cure the original disease by surgical intervention the second di ease developed This group of case of combined ileocolitis may be called metachronou in nature signifying that the combined di eases succeeded or followed each other There were 4 cases of granulomatous ileocolitis one with extensive involvement of the colon including the rectum one with extensive involvement of the colon excepting the rectum and two with the granulomatous process localized to the a cending colon only (fig 77 and 78)

Etiology

The age and sex distribution of ileocolitis i similar to that of the two independent diseases The age incidence ranged from 9 to 70 years with the average or mean age being 26 5 There were 29 female and 35 males

The pathologic di tribution of the involved segments in ileocolitis are so variable and heterogenous that an exact clas ification is impo sible The following table i an attempt to clas ify the 45 ca e of synchronou ileocolitis —

TABLE 20

Terminal ileum and proximal colon	19 cases
Terminal ileum and transverse colon	2
Terminal ileum and whole or distal colon to sigmoid	12
Ileum and jejunum and whole colon	6
Terminal ileum and distal colon	5
Terminal ileum and entire colon including rectum	1
Total	45 case

It i important to note in the study of the life cycle of ca es of segmental colitis that the inflammatory process spread distally from the proximal colon the proce s stopping or tarrying for long period of time at the sigmoid flexure extending into the rectum rarely only late in the course of an intractable and particularly virulent type of invasion and progression However the rectum is not immune In several cases

including two fatal instances that succumbed after multiple and unsuccessful resections the terminal phase was marked by a severe proctitis In four other living cases it was necessary to resort to ileo tomy as a life saving measure to prevent the patient from succumbing to a severe proctitis with its frequent rectal complications

Clinical Features

Diarrhea cramp and fever are the most common symptoms of ileocolitis Cramps and diarrhea are almost always present Fever is present during the acute or active phases of the disease ranging from 101 F to 102° F in the low grade cases in acute toxic ca es the temperature may reach as high as 106° F Leukocytosis with poly nucleosis corresponds to the fever with leukocyte counts ranging from 12 000 to 16 000 per cubic millimeter and occasionally reaching 20 000 However counts below 10 000 per cubic millimeter with a high poly nucleosis and many young unsegmented polymorphonuclear leukocyte with toxic granulations are frequently found in the acute cases The sedimentation rate correspond to the fever and to the leukocytosis but usually remains elevated during the afebrile periods until the inflamma tion completely ubsides Foul diarrhea with or without bloody stools and cramps is usually present but the tenesmus and rectal urgency found in universal ulcerative colitis are absent In four cases there was an absence of diarrhea and even constipation was noted Gross fresh hemorrhage per rectum was present in 11 instances and was massive producing shock in 3 cases melena was noted twice

Severe anorexia and progressive weight loss occur during the acute recurrences and in extreme cases losses of 50 to 60 pounds may occur producing severe malnutrition and cachexia Signs of vitamin B deficiency are especially frequent with gloss tis and rhagades being the most fre quent Deficiency of vitamin K causing bleeding due to increased proth rombin time is found in the more intractable cases An elevated alkaline phosphatase has been noted in several in tances in the serum but its significance is not yet understood perhaps th s is related to liver damage wh ch in itself may lead to a vitamin K defi iency Secondary anemia is consistently pre ent with he hemoglobin level ranging between 9 and 11 grams per 100 cc In the febrile cases with hemoconcentration the hemoglobin values may be normal so that it is important to check them with hematocrit readings Hypoproteinemia i the rule but is usually mild in the more protracted cases the protein value may drop to 3 2 grams with a marked decrease in the serum albumen causing a reversal

in the album n globulin ratio Hypocalcemia and tetany were ob erved in only 3 cases Arthriti was present in 18 instance u ually involving the larger joints An associated duodenal ulcer was present in 7 patient and the history of infectious mononucleosis was noted in 3 instances

An abdominal mass was palpable in 26 instances usually placed in the right lower quadrant Splenomegaly was noted in 4 instance and clubbing of the fingers was present in 6 cases Erythema nodosum occurred 17 times in the lower extremities and stomatitis with ulcerative pharyngitis twice Phlyctenular conjunctivitis wa noted once Intestinal obstruction causing abdominal di tention and fluid levels in the small intestine occurs rarely and usually subsides after intestinal intubation

Internal fistulas originating in the di ease l terminal ileum extend



FIG. 79 Granul matous l oc l t invol ng t rminal ile m and ascend ng c lon

including two fatal instances that succumbed after multiple and unsuccessful resections the terminal phase was marked by a severe proctitis In four other living cases it was necessary to resort to ileostomy as a life saving measure to prevent the patient from succumbing to a severe proctitis with its frequent rectal complications

Clinical Features

Diarrhea cramp and fever are the most common symptoms of ileocolitis Cramps and diarrhea are almost always present Fever is present during the acute or active phases of the disease ranging from 101 F to 102 F in the low grade cases in acute toxic cases the temperature may reach as high as 106 F Leukocytosis with polynucleosis corresponds to the fever with leukocyte counts ranging from 12 000 to 16 000 per cubic millimeter and occasionally reaching 20 000 However counts below 10 000 per cubic millimeter with a high polynucleosis and many young unsegmented polymorphonuclear leukocytes with toxic granulations are frequently found in the acute cases The sedimentation rate correspond to the fever and to the leukocytosis but usually remains elevated during the afebrile periods until the inflammation completely subsides Foul diarrhea with or without bloody stool and cramps is usually present but the tenesmus and rectal urgency found in universal ulcerative colitis are absent In four ca es there was an absence of diarrhea and even constipation was noted Gross fresh hemorrhage per rectum was present in 11 instances and was massive producing shock in 3 cases melena was noted twice

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FIG 81 Combined ileocolitis resected specimen

Medical Therapy

Medical treatment is the first choice and should be attempted in all cases of ileocolitis unless there are definite and well defined indication for surgical intervention As in the simple cases of ileitis or ulcerative colitis the essential part of the therapy consists of supportive therapy including bed rest a high protein bland low residue diet intravenous fluid and plasma or blood whenever necessary to restore normal blood values We find injections of crude liver extract and vitamin B complex to be very helpful

The insoluble sulfonamide and antibiotics such as tetracycline and dihydrostreptomycin are used to combat secondary infection Penicillin is of no value for the treatment of this disease and its complications However steroid therapy has been of definite value and is especially effective in the acute stages of high fever and intoxication This is best administered in the form of corticotropin (Acthar) gel parenterally or in the newer long acting zinc corticotropin preparation that need to be administered only once in 48 to 72 hours Once the desired improvement is obtained the steroid therapy may then be continued with prednisone (Meticorten) or hydrocortisone (Hydrocorten) orally In many

to the cecum and other parts of the colon in 10 cases and in one instance a jejuno ileal fistula occurred External fecal fistulas to the anterior abdominal wall complicated 7 cases Four of these fecal fistulas were secondary to a perforated ulcerative colitis of the sigmoid and 2 fistulas originated in the terminal ileum Rectal complications were frequent

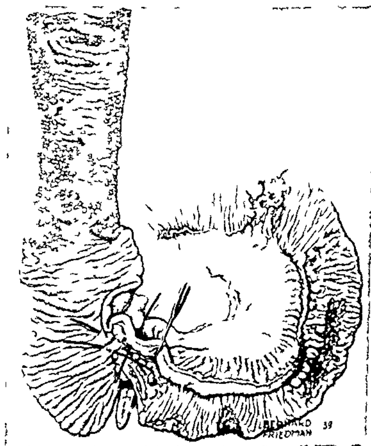


FIG 80 Combined ileocolitis granulomatous ileitis with fistulas and ulcerative colitis with pseudopolyposis

perirectal abscesses and fistula were present in 25 cases 4 cases were associated with rectovaginal fistulas and in one male there was a deep recto urethral fistulous tract

he is well and weighs 190 lbs (86 Kg) In two case of terminal ileitis and proctiti an ileotran verse colo tomy was performed followed by progres ion of the coliti with perianal absces es finally neces itating ileos tomy In 10 ca e ileocolic resection and ileosigmoidostomy were per formed for terminal ileiti and right sided colitis Of these patient 4 required ileostomy after the rectum became involved 3 patient definitely are improved 2 are in poor condition due to recurrent di ea e the last has just been operated on

One case of terminal ileiti wa associated with a granulomatou colitis involving the entire colon including the rectum Exactly two year prior to the time of writing a total colectomy and resection of the terminal ileum was performed at one stage and the pathologic speci men revealed typical granulomatou ileitis associated with a thickened colon containing giant cell systems and epithelioid tubercles suggesting the diagnosis of granulomatous coliti the patient made an uneventful recovery and gained 40 lb with a permanent ileostomy

In two cases a diffu e ileojejuniti was associated with a diffu e ulcerative coliti involving the entire colon excepting the rectum In one patient an ileosigmoidostomy and subtotal colectomy were performed he continues in poor nutrition with acute exacerbations of fever and diarrhea due to the residual ileojejunitis The second patient has been observed for 18 years and presents the life history of ileojejunitis and right-sided coliti with the gradual progre ion of the disease to involve the entire colon In this patient the clinical course began with a terminal ileitis and proximal colitis at the age of 20 years subsequently he developed a diffuse ileojejuniti with a gradual extension of the colitis to involve the entire colon including the rectum Over the course of 16 years multiple resections of the small and large intestine were per formed and at present he is left with an ileostomy situated 7 feet from the ligament of Treitz His serum electrolytes and hemoglobin are stabilized at normal levels hi weight is constant and he i re tored to working efficiency A typical granulomatous ileiti was reported by pathologic examination of the specimen the ascendin colon revealed a chronic hyperplastic and polypoid colitis The remainin part of the transverse and descending colon including the rectum revealed a typical chronic ulcerative colitis (fig 79)

Metachr nous Ileocolitis There were 19 cases of metachronous ileocolitis Fourteen of these originated as terminal ileitis the ulcerative colitis developing after an ileotran verse colostomy (with or without ileo-

instances results of the oral use of steroids are disappointing because of their poor absorption One patient with diffuse disease of the small and large intestine made a remarkable recovery gaining 30 lb (14 kg) and was able to resume his work as a mail carrier after treatment with corticotropin gel daily to prevent the recurrence of his symptoms Another patient 70 years of age with high temperature marked intoxication and erythema nodosum of the legs became asymptomatic after six injections of corticotropin

Of the 18 patients treated medically one is cured 2 are well 5 are improved and 8 continue to have frequent recurrences and are in a chronic state of malnutrition One patient died at the age of 70 and one patient was lost to follow up The patient who was cured had a typical terminal ileitis with concurrent involvement of the transverse colon He was treated with nonspecific protein shock therapy in the form of typhoid vaccine given intravenously He showed a dramatic response and four years later x ray examination revealed a normal mucous membrane throughout the entire colon and a slight distortion of the terminal ileum 18 years after the original illness the man is well

Surgical Management

In this series 46 patients were treated surgically multiple operations being required in most instances The surgical approach to the treatment of ileocolitis presents numerous and complex problems even to the most experienced surgeon In general surgical intervention is most successful where the disease is localized to the distal part of the ileum and proximal part of the colon and the patient has not responded to medical therapy Local palliative resections of stenotic diseased areas of ileitis and jejunitis are frequently necessary when intestinal obstruction exists Occasionally massive resections of the colon and small intestine have been necessary because of exsanguinating hemorrhage or progressive disease

Synchronous Ileocolitis There were 27 cases of synchronous ileocolitis treated surgically In 14 of these cases the disease was limited to the terminal ileum and ascending colon Ileocolic resection was performed in 11 and a short circuiting procedure (ileotransverse colectomy) in the other 3 instances Results were good in 7 cases poor in 6 due to recurrent disease one patient died after a secondary resection

In the remaining 13 cases one patient had an ileosigmoidostomy with transection of the ileum for terminal ileitis and transverse colitis

he is well and weigh 190 lb (86 Kg) In two case of terminal ileiti and proctitis an ileotransverse colo tomy was performed followed by progres ion of the coliti with perianal absce es finally necessitating ileos tomy In 10 ca e ileocolic resection and ileosigmoido tomy were per formed for terminal ileiti and right sided colitis Of the e patient 4 required ileo tomy after the rectum became involved 3 patient definitely are improved 2 are in poor condition due to recurrent di ease the last ha just been operated on

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lomatous ileiti proximal to the ileosigmoidostomy 46 cm of terminal ileum was re ected and granulomatou ileitis with fistula formation was revealed She had a normal full term pregnancy three years ago however during the eighth month of her second pregnancy she had a recurrence of fever and diarrhea and at the time of ce arean se tion ten months ago acute ileitis was seen proximal to the site of the anastomosi Becau e of recurrent intestinal obstruction 18 inches of granulomatous ileitis was resected three months ago The patient now weighs 115 lb has only three to four stool a day and is an active hou ewife de pite the presence of a high ileosigmoidostomy

The fifth patient with a subtotal colectomy and ileosigmoidostomy for right sided ulcerative colitis developed proctitis requiring ileostomy At this time a segment of granulomatous jejunitis 18 inches in extent was resected Six years lat r she developed granulomatous ileiti involving the terminal 24 inches of ileum immediately proximal to the site of the ileo tomy Both the jejuniti and the ileitis were typically granulomatous containing skip lesions and did not resemble the superfi ial ulcerative ileitis frequently seen after ileo tomy This ulcerative ileitis is prone to occur when there is stenosi of the ileostomy toma causing obstruction This complication has occurred 5 times in our experience In addition we have had 2 patients in whom ileo tomy was performed who developed oon the efter a severe necrotizing diffuse ileojejunitis with a fulminating clinical course complicated by ma sive hemorrhage and with a fatal outcome within 48 hours

Prognosis and Results

Of the 18 patients treated medically 3 are well and 5 are improved but 8 are in poor condition with frequent recurrences One patient died and one patient was lost to follow up Results in the 46 surgical case can be considered good in only 12 patients 8 improved 21 are poor 2 died and 3 patients are lo t to follow up Fourteen of these surgical patients eventually required permanent ileostomy As expected the progno is in the combination of the e two severe inflammatory diseases is poor When the di ease remains localized to the terminal ileum and small adjacent egm nts of the colon the results ar gen rally good Many of the e patients in our series had complicated ca es and had been referred to our office after previou unsuccessful attempt at medical or surgical cure

After 25 years of experience in handling these complicated cases

colic resection) had been performed In one case the secondary coliti was restricted to the transverse colon and after a subsequent resection the patient was well A second patient after a short circuiting procedure for terminal ileitis developed diffuse ulcerative colitis but his disease has been in a continuous remission for the past five years Two other patients after an ileocolic resection for ileitis developed a mild but persistent ulcerative colitis In another case death followed infection with clostridia one patient was lost to follow up The remaining 8 patients who originally had terminal ileitis developed a subsequent ulcerative colitis after surgical intervention for the cure of the ileitis In all 8 patients the subsequent ulcerative colitis has been severe requiring ileostomy in three instances One of the latter cases began with a terminal ileitis when the patient was 28 years of age After an ileotransverse colostomy and subsequent ileocolic resection including 4 feet of diseased terminal ileum there was marked improvement for seven years He then developed increased diarrhea associated with chills and fever barium enema three years ago revealed ulcerative colitis involving the sigmoid and lower part of the descending colon Despite intensive treatment including steroid therapy his course was downhill and resection of the entire distal part of the colon including the rectum was required for severe advanced ulcerative coliti causing massive hemorrhage At present the ileostomy drainage averages 3 liters but the patient's weight is stabilized at 130 lb (59 Kg) and his blood electrolytes are within normal range without intravenously given supplements

The other 5 cases of metachronous ileocolitis began with right sided ulcerative coliti for which subtotal colectomy with ileosigmoidostomy was performed In 2 of these cases the resected terminal ileum was normal the other 3 cases presented the typical backwash ileiti Within five years a true granulomatous ileitis developed in 4 of these patients in the new terminal ileum proximal to the site of the ileosigmoidostomy Of these 4 patient 2 required subsequent ileostomy due to rectal complications and are well now A third patient developed mild proctitis and duodenal ulcer The fourth case is significant because granulomatou *ileitis recurred twice after resection for right sided ulcerative* coliti and yet the sigmoid and rectum are still perfectly normal This patient is now 28 year of age at the age of 18 she underwent a subtotal colectomy and ileosigmoidostomy for right sided ulcerative colitis with a fecal fistula to the abdominal wall Five year later she developed recurrent symptom and radiographic studies revealed a typical granu

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of combined ileocolitis one learns the value of a conservative medical approach Expectant therapy should be the treatment of choice unless there are urgent surgical indications such as recurrent massive hemorrhage recurrent bouts of intestinal obstruction or persistent fistulas We have found steroid therapy especially in the form of corticotropin injection of definite value in causing remissions and maintaining sustained improvement The best surgical results in our series were obtained when the patients had been observed for a long period of time and the disease *remained localized to the distal part of the ileum and proximal part* of the colon Recurrences have followed invariably when the patient was operated on during the diffuse stages and the surgeon was unable to delimit the segments of involved disease In the presence of diffuse disease multiple resections of localized segments causing active symptom will often bring about marked remission and slowly enable the remainder of the intestine to take over the absorptive function However in some instances massive resections of the small and large intestine may be necessary these are now possible with satisfactory results after preoperative preparation with multiple transfusions and antibiotics

In these confusing complicated often bewildering forms of combined disease (ileitis and colitis or ileocolitis) no absolute rule can be laid down for the approach to surgical therapy Every case must be considered on an individual basis since there are so many variant and so many possible combinations of the different factors Where medical therapy fails where fistula formations abdominal masses perirectal abscesses and fistula persist where gross massive hemorrhage or obstruction of the small intestine supervenes one has no choice but to ask for radical surgical interference And this in face of the fact that radical surgical intervention seems to offer little but amelioration and is so often followed by disappointing recurrences or by spread of the disease to new anatomic territories Medical cures or permanent cures under conservative therapy are very few

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